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Inventor search

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L1          558 SEA FILE=CAPLUS ABB=ON  BRANDT J?/AU
L2          152 SEA FILE=CAPLUS ABB=ON  FARID N?/AU
L3          261 SEA FILE=CAPLUS ABB=ON  JAKUBOWSKI J?/AU
L4           89 SEA FILE=CAPLUS ABB=ON  WINTERS K?/AU
L5            2 SEA FILE=CAPLUS ABB=ON  L1 AND L2 AND L3 AND L4


=> fil medl jic wpix biosis embase; d que l13; d que l14; s l13 or l14
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L8         2404 SEA BRANDT J?/AU
L9          772 SEA FARID N?/AU
L10         629 SEA JAKUBOWSKI J?/AU
L11         371 SEA WINTERS K?/AU
L13           3 SEA L8 AND L9 AND L10 AND L11



L8         2404 SEA BRANDT J?/AU
L9          772 SEA FARID N?/AU
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Searched by Barb O'Bryen, STIC 2-2518

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L10          629 SEA JAKUBOWSKI J?/AU
L11          371 SEA WINTERS K?/AU
L12        55838 SEA PERCUTANEOUS?(5A) CORONARY
L14           16 SEA (L8 OR L9 OR L10 OR L11) AND L12


L15          18 L13 OR L14

=> dup rem l5,l15
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PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L15
L16           13 DUP REM L5 L15 (7 DUPLICATES REMOVED)
                 ANSWERS '1-2' FROM FILE CAPLUS
                 ANSWERS '3-7' FROM FILE MEDLINE
                 ANSWERS '8-13' FROM FILE BIOSIS

=> d ibib ed abs 1-2; d iall 3-13

L16  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:366820  CAPLUS
TITLE:                    The Platelet Inhibitory Effects and Pharmacokinetics
                          of Prasugrel After Administration of Loading and
                          Maintenance Doses in Healthy Subjects
AUTHOR(S):                Jakubowski, Joseph A.; Payne, Christopher
                          D.; Brandt, John T.; Weerakkody, Govinda J.;
                          Farid, Nagy A.; Small, David S.; Naganuma,
                          Hideo; Li, Grace Ying; Winters, Kenneth J.
CORPORATE SOURCE:         Lilly Research Laboratories, Eli Lilly and Company,
                          Indianapolis, IN, 46285, USA
SOURCE:                   Journal of Cardiovascular Pharmacology (2006), 47(3),
                          377-384
                          CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER:                Lippincott Williams & Wilkins
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  21 Apr 2006
AB   Prasugrel (CS-747, LY640315), a novel thienopyridine, is a potent and
     orally active antiplatelet agent in vivo.  The aims of this double-blind,
     double-dummy, placebo-controlled, randomized, parallel group phase 1 study
     were to investigate the antiplatelet effects of prasugrel after oral
     administration of a loading dose (LD) and subsequent 20 days of once-daily
     maintenance dosing (MD), to characterize the pharmacokinetics of prasugrel
     metabolites with an LD/MD regimen, and to assess the safety and
     tolerability of prasugrel in healthy subjects.  Subjects were randomly
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assigned in a 1:1:1 ratio to prasugrel 40 mg LD/7.5 mg MD (n=11), prasugrel 60 mg LD/15 mg MD (n=10), or placebo LD/placebo MD (n=11). Prasugrel 40 and 60 mg LDs provided rapid and consistent inhibition of 20 μM ADP-stimulated platelet aggregation. Prasugrel 7.5 and 15 mg MDs maintained inhibition in a dose-dependent manner. The pharmacokinetic data indicate that exposure to prasugrel metabolites occurs rapidly after dosing and is consistent with dose proportionality. Within the limitations of this study, the safety and tolerability results suggest that prasugrel is well tolerated when dosed as an initial LD followed by a lower daily MD for 20 days. Prasugrel LDs and MDs provide rapid and sustained inhibition of ADP-mediated platelet aggregation.

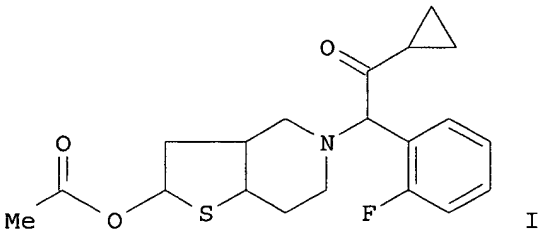
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:996025 CAPLUS
DOCUMENT NUMBER: 141:428013
TITLE: 2-Acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine pharmaceuticals for treating cardiovascular disease
INVENTOR(S): **Brandt, John Thomas; Farid, Nagy Alphonse; Jakubowski, Joseph Anthony; Winters, Kenneth John**
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098713	A2	20041118	WO 2004-US11257	20040426
WO 2004098713	A3	20041229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1660183	A2	20060531	EP 2004-750031	20040426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-467903P P 20030505
WO 2004-US11257 W 20040426

ED Entered STN: 19 Nov 2004
GI



I

AB A method of treating cardiovascular diseases comprising administering I or a pharmaceutically acceptable salt, solvate, prodrug, active metabolite, racemate or enantiomer thereof, in conjunction with coronary and non-coronary intervention procedures is disclosed. I was prepared and formulated into tablets or capsules.

L16 ANSWER 3 OF 13 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005331652 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15967851
TITLE: Randomized comparison of prasugrel (CS-747, LY640315), a novel thienopyridine P2Y12 antagonist, with clopidogrel in **percutaneous coronary** intervention: results of the Joint Utilization of Medications to Block Platelets Optimally (JUMBO)-TIMI 26 trial.
AUTHOR: Wiviott Stephen D; Antman Elliott M; **Winters Kenneth J**; Weerakkody Govinda; Murphy Sabina A; Behounek Bruce D; Carney Robert J; Lazzam Charles; McKay Raymond G; McCabe Carolyn H; Braunwald Eugene
CORPORATE SOURCE: TIMI Study Group, Cardiovascular Division, Brigham and Women's Hospital, Department of Medicine, Harvard Medical School, Boston, Mass 02115, USA. (JUMBO-TIMI 26 Investigators). swiviott@partners.org
SOURCE: Circulation, (2005 Jun 28) Vol. 111, No. 25, pp. 3366-73. Electronic Publication: 2005-06-20. Journal code: 0147763. E-ISSN: 1524-4539.
COMMENT: Comment in: Evid Based Cardiovasc Med. 2005 Dec;9(4):301-4. PubMed ID: 16380060
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL, PHASE II) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL) (CLINICAL TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200602
ENTRY DATE: Entered STN: 29 Jun 2005 Last Updated on STN: 4 Feb 2006 Entered Medline: 3 Feb 2006

ABSTRACT:
BACKGROUND: Despite the current standard antiplatelet regimen of aspirin and clopidogrel (with or without glycoprotein IIb/IIIa inhibitors) in ***percutaneous*** **coronary** intervention patients, periprocedural and postprocedural ischemic events continue to occur. Prasugrel (CS-747, LY640315), a novel potent thienopyridine P2Y(12) receptor antagonist, has the potential to achieve higher levels of inhibition of ADP-induced platelet

aggregation than currently approved doses of clopidogrel. METHODS AND RESULTS: Joint Utilization of Medications to Block Platelets Optimally-Thrombolysis In Myocardial Infarction 26 (JUMBO-TIMI 26) was a phase 2, randomized, dose-ranging, double-blind safety trial of prasugrel versus clopidogrel in 904 patients undergoing elective or urgent **percutaneous coronary** intervention. Patients were randomized to either standard dosing with clopidogrel or 1 of 3 prasugrel regimens. Subjects were monitored for 30 days for bleeding and clinical events. The primary end point of the trial was clinically significant (TIMI major plus minor) non-CABG-related bleeding events in prasugrel- versus clopidogrel-treated patients. Hemorrhagic complications were infrequent, with no significant difference between patients treated with prasugrel or clopidogrel in the rate of significant bleeding (1.7% versus 1.2%; hazard ratio, 1.42; 95% CI, 0.40, 5.08). In prasugrel-treated patients, there were numerically lower incidences of the primary efficacy composite end point (30-day major adverse cardiac events) and of the secondary end points myocardial infarction, recurrent ischemia, and clinical target vessel thrombosis. CONCLUSIONS: In this phase 2 study, which was designed to assess safety when administered at the time of **percutaneous coronary** intervention, prasugrel and clopidogrel both resulted in low rates of bleeding. The results of this trial serve as a foundation for the large phase 3 clinical trial designed to assess both efficacy and safety.

CONTROLLED TERM: Check Tags: Female; Male
Adolescent
Adult
Aged
***Angioplasty, Transluminal, Percutaneous Coronary: AE, adverse effects**
Angioplasty, Transluminal, Percutaneous Coronary: MT, methods
Cardiovascular Diseases: PC, prevention & control
Comparative Study
Dose-Response Relationship, Drug
Double-Blind Method
Hemorrhage: CI, chemically induced
Humans
Incidence
*Membrane Proteins: AI, antagonists & inhibitors
Middle Aged
*Piperazines: AD, administration & dosage
Piperazines: TO, toxicity
*Platelet Aggregation Inhibitors: AD, administration & dosage
Platelet Aggregation Inhibitors: TO, toxicity
Pyridines: AD, administration & dosage
Pyridines: TO, toxicity
*Receptors, Purinergic P2: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
*Thiophenes: AD, administration & dosage
Thiophenes: TO, toxicity
Ticlopidine: AD, administration & dosage
*Ticlopidine: AA, analogs & derivatives
Ticlopidine: TO, toxicity

CAS REGISTRY NO.: 55142-85-3 (Ticlopidine); 90055-48-4 (clopidogrel)

CHEMICAL NAME: 0 (Membrane Proteins); 0 (P2RY12 protein, human); 0 (Piperazines); 0 (Platelet Aggregation Inhibitors); 0 (Pyridines); 0 (Receptors, Purinergic P2); 0 (Thiophenes); 0 (prasugrel); 0 (purinoceptor P2Y12); 0 (thienopyridine)

L16 ANSWER 4 OF 13 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 97057313 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8901652
TITLE: Association of heparin-resistant thrombin activity with acute ischemic complications of coronary interventions.
AUTHOR: Oltrona L; Eisenberg P R; Lasala J M; Sewall D J; Shelton M E; **Winters K J**
CORPORATE SOURCE: II Divisione Cardiologica, Ospedale Niguarda, Milano, Italy.
CONTRACT NUMBER: HL-17646 (NHLBI)
SOURCE: Circulation, (1996 Nov 1) Vol. 94, No. 9, pp. 2064-71. Journal code: 0147763. ISSN: 0009-7322.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 6 Dec 1996

ABSTRACT:
BACKGROUND: Acute thrombosis is thought to contribute to abrupt ***coronary*** occlusion during **percutaneous coronary** revascularization despite the administration of heparin and aspirin. This study was designed to detect the presence of heparin-resistant thrombin activity and to define its relationship to the acute ischemic complications of coronary interventions. METHODS AND RESULTS: Plasma levels of fibrinopeptide A (FPA) and prothrombin fragment 1.2 (F1.2), markers of thrombin and factor Xa activity, respectively, were measured in the coronary sinus with heparin-bonded catheters in 58 patients undergoing coronary interventions. Activated coagulation times were maintained > 300 seconds by the Hemochron method. Mean FPA levels decreased significantly, from 7.0 +/- 0.9 nmol/L before the procedure to 5.2 +/- 0.5 nmol/L after the heparin bolus and to 2.9 +/- 0.2 nmol/L after the procedure (P = .0001). In 26 patients (45%), FPA levels remained above the threshold for suppression angioplasty of thrombin activity determined during angiography in 7 patients without coronary artery disease (> 3.0 nmol/L). FPA concentrations after coronary interventions were increased in patients with intracoronary thrombus (P = .01), abrupt coronary occlusion (P = .06), postprocedural non-Q-wave myocardial infarction (P = .04), and clinically unsuccessful procedures (P = .04). F1.2 levels were relatively low before the procedures and did not change significantly. CONCLUSIONS: Heparin administration suppresses thrombin activity in most but not all patients undergoing coronary interventions. Heparin-resistant thrombin activity is associated with angiographic evidence of intracoronary thrombus and ischemic complications of coronary interventions.

CONTROLLED TERM: Check Tags: Female; Male
Acute Disease
Aged
Angiography
Blood Specimen Collection
Factor Xa: AI, antagonists & inhibitors
Fibrinopeptide A: ME, metabolism
*Heart Catheterization: AE, adverse effects
*Heparin: PD, pharmacology
Humans
Middle Aged
*Myocardial Ischemia: CO, complications
Myocardial Ischemia: ET, etiology
Myocardial Ischemia: ME, metabolism
Peptide Fragments: ME, metabolism
Prothrombin: ME, metabolism
Reproducibility of Results

Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*Thrombin: AI, antagonists & inhibitors
*Thrombin: ME, metabolism
Thrombosis: DT, drug therapy
Thrombosis: ET, etiology
Whole Blood Coagulation Time
CAS REGISTRY NO.: 25422-31-5 (Fibrinopeptide A); 9001-26-7 (Prothrombin); 9005-49-6 (Heparin)
CHEMICAL NAME: 0 (Peptide Fragments); 0 (prothrombin fragment 1.2); EC 3.4.21.5 (Thrombin); EC 3.4.21.6 (Factor Xa)

L16 ANSWER 5 OF 13 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 85254899 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3160477
TITLE: Failure of **percutaneous** transluminal **coronary** angioplasty to stimulate platelet and prostaglandin activity.
AUTHOR: Stine R A; Magorien R D; Bush C A; Kolibash A J; Leier C V; Fertel R H; **Brandt J**; Unverferth D V
SOURCE: Catheterization and cardiovascular diagnosis, (1985) Vol. 11, No. 3, pp. 247-54.
Journal code: 7508512. ISSN: 0098-6569.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198508
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 26 Aug 1985

ABSTRACT:
Platelet function and prostaglandin activity were evaluated in nine patients with **coronary** artery disease undergoing **percutaneous** left anterior descending **coronary** artery angioplasty (PTCA) and compared to nine normal controls. Transcoronary measurements (arterial-coronary sinus) of platelet counts, mean platelet volume, platelet factor 4 (PF4), beta thromboglobulin, thromboxane (B2), and 6-keto-PGF 1 alpha were made. When compared to normal controls, the patients with coronary artery disease had higher circulating baseline levels of PF4 in the coronary sinus. There was no transcardiac production of any factor at baseline or immediately after infusion of nitroglycerin or performance of PTCA. These results suggest that PTCA does not grossly alter arachidonic acid metabolism or platelet activity.
CONTROLLED TERM: 6-Ketoprostaglandin F1 alpha: BL, blood
Adult
Aged
*Angioplasty, Balloon
Coronary Disease: BL, blood
*Coronary Disease: TH, therapy
Heart Catheterization
Humans
Middle Aged
*Platelet Aggregation
Platelet Count
Platelet Factor 4: PH, physiology
*Prostaglandins: BL, blood
Research Support, Non-U.S. Gov't
Thromboxane B2: BL, blood
beta-Thromboglobulin: ME, metabolism
CAS REGISTRY NO.: 37270-94-3 (Platelet Factor 4); 54397-85-2 (Thromboxane

B2); 58962-34-8 (6-Ketoprostaglandin F1 alpha)
CHEMICAL NAME: 0 (Prostaglandins); 0 (beta-Thromboglobulin)

L16 ANSWER 6 OF 13 MEDLINE on STN
ACCESSION NUMBER: 1999030710 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9812911
TITLE: Effects of beta3-integrin blockade (c7E3) on the response to angioplasty and intra-arterial stenting in atherosclerotic nonhuman primates.
AUTHOR: Deitch J S; Williams J K; Adams M R; Fly C A; Herrington D M; Jordan R E; Nakada M T; **Jakubowski J A**; Geary R L
CORPORATE SOURCE: Departments of Surgery and Comparative Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, USA.
CONTRACT NUMBER: HL49488 (NHLBI)
P01-HL45666 (NHLBI)
R01-HL57557 (NHLBI)
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, (1998 Nov) Vol. 18, No. 11, pp. 1730-7.
Journal code: 9505803. ISSN: 1079-5642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 10 Dec 1998

ABSTRACT:
Because the beta3-antagonist abciximab (c7E3 Fab) has significantly improved late outcomes after coronary angioplasty, the beta3 integrins have been implicated in the arterial response to injury. However, the mechanisms underlying this benefit are unknown. The observation that c7E3 binds beta3 integrins on vascular cells (alphavbeta3) with affinity equal to that for the platelet glycoprotein IIb/IIIa integrin has led to the hypothesis that c7E3 may act directly on the artery wall to prevent restenosis after angioplasty. To test this hypothesis, we studied the effects of c7E3 on structural changes within the artery wall after angioplasty or stent angioplasty in 23 male cynomolgus monkeys with established atherosclerosis. Animals were randomly assigned to receive either a bolus of c7E3 (0.4 mg/kg IV, n=11) followed by a 48-hour infusion (0. 2 microg. kg-1. min-1) or an equal volume of vehicle (n=12). Animals received weight-adjusted aspirin and heparin and then underwent unilateral iliac artery experimental angioplasty and subclavian artery stent angioplasty (Palmaz). Iliac artery lumen diameter (LD) was determined by angiography at baseline (LDPre), after angioplasty (LDPost), and 35 days later (LDDay35). Arteries were then fixed by perfusion and removed for analysis. Lumen, intima, media, and external elastic lamina (EEL) areas were measured in iliac artery cross sections. Values from each injured iliac artery were normalized to the contralateral uninjured iliac artery to control for interanimal variability in baseline artery size and atherosclerosis extent. Intimal area was also measured in subclavian stent cross sections. c7E3 blocked platelet aggregation and prolonged the bleeding time from 2.8+/-1.1 to 19.8+/-2.5 minutes, P<0.001. Experimental angioplasty increased LDPost an average of 28%, and the initial gain was similar in both groups (P=NS). Despite an anti-platelet effect, c7E3 did not inhibit iliac lumen narrowing (LDDay35-LDPost: c7E3, -0.69+/-0.17 versus vehicle, -0.99+/-.17 mm, P=0.35); intimal hyperplasia (neointima area: c7E3, 1.12+/-.28 versus vehicle, 1.22+/-.20 mm2, P=0.77); or decrease in artery wall size (EEL area [percent of uninjured control]: c7E3, 101+/-7% versus vehicle, 121+/-7%). Stent intimal

hyperplasia was also unaltered by c7E3 treatment (neointimal area: c7E3, 1.09+/-0.16 versus vehicle, 1. 28+/-0.11 mm2, P=0.36). These results suggest that the benefits of c7E3 treatment in coronary angioplasty were not from inhibition of intimal hyperplasia or improved artery wall remodeling. Alternative mechanisms should be explored to explain improved late outcomes after angioplasty in patients treated with c7E3.

CONTROLLED TERM: Check Tags: Male
***Angioplasty, Transluminal, Percutaneous Coronary**
Animals
*Antibodies, Monoclonal: TU, therapeutic use
Arteries
*Arteriosclerosis: TH, therapy
Blood Coagulation: DE, drug effects
Combined Modality Therapy
Drug Evaluation, Preclinical
Hematologic Tests
Hyperplasia: DT, drug therapy
*Immunoglobulin Fab Fragments: TU, therapeutic use
*Integrins: AI, antagonists & inhibitors
Lipids: BL, blood
Macaca fascicularis
*Platelet Aggregation Inhibitors: TU, therapeutic use
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Stents
Treatment Outcome

CAS REGISTRY NO.: 143653-53-6 (abciximab)

CHEMICAL NAME: 0 (Antibodies, Monoclonal); 0 (Immunoglobulin Fab Fragments); 0 (Integrins); 0 (Lipids); 0 (Platelet Aggregation Inhibitors)

L16 ANSWER 7 OF 13 MEDLINE on STN

ACCESSION NUMBER: 95216989 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7702414

TITLE: [Angioscopic evaluation of the immediate result of coronary angioplasty in relation to balloon inflation time]. Evaluation angioscopique du resultat immediat de l'angioplastie coronaire en fonction de la duree des gonflages du ballonnet.

AUTHOR: Eltchaninoff H; Cribier A; Koning R; Jolly N; Baala B; **Farid N**; Letac B

CORPORATE SOURCE: Service de cardiologie, hopital Charles-Nicolle, CHU de Rouen.

SOURCE: Archives des maladies du coeur et des vaisseaux, (1994 Jun) Vol. 87, No. 6, pp. 721-7.
Journal code: 0406011. ISSN: 0003-9683.

PUB. COUNTRY: France

DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199505

ENTRY DATE: Entered STN: 10 May 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 2 May 1995

ABSTRACT:
The aim of this study was to assess the effects of coronary angioplasty on the intima with respect to the duration of balloon inflation by percutaneous angioplasty. Twenty-seven patients were randomized according to the total

duration of balloon inflation: Group I "standard" duration (total duration < or = 3 min, N = 13) and Group II: prolonged duration (total duration > or = 12 min, N = 14); the type and distribution of the lesions were comparable in the two groups. The results of angioplasty were evaluated immediately after dilatation by angiography and angioscopy. Angioscopy was performed without failure or complications with perfect definition of the images in all cases. Angioscopy showed 1) intimal tears, 2) thrombi, 3) longitudinal dissections. A classification in three grades was used taking the apparent gravity of the lesions into consideration. The mean duration of balloon inflation in Group I was 205 +/- 45 s and 958 +/- 129 s in Group II. The residual stenosis was 36 +/- 8% in Group I and 26 +/- 10% in Group II ($p < 0.05$). Angioscopy showed the frequency of intimal tears to be twice greater in Group I (9 cases) than in Group II (4 cases) ($p = 0.05$). Intravascular thrombi were observed in 13 cases, 6 in Group I and 7 in Group II. One case of longitudinal dissection was observed in each group: only one of these two cases was detected at angiography. The authors conclude that repeated and prolonged balloon inflations improve the immediate results of angioplasty with less residual stenosis at angiography and a lower incidence of intimal tears at angioscopy.

CONTROLLED TERM: Check Tags: Female; Male
Aged
***Angioplasty, Transluminal, Percutaneous Coronary**
*Angioscopy
*Coronary Disease: TH, therapy
*Coronary Vessels
English Abstract
Humans
Image Processing, Computer-Assisted
Middle Aged
Random Allocation
Time Factors

L16 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:182137 BIOSIS
DOCUMENT NUMBER: PREV200600184249
TITLE: Prasugrel (CS-747, LY640315) hydrochloride, a novel thienopyridine prodrug, shows potent antiplatelet and antithrombotic effects with rapid onset of action in rats.
AUTHOR(S): Niitsu, Yoichi [Reprint Author]; Ogawa, Taketoshi; Sugidachi, Atsuhiro; **Jakubowski, Joseph A.**; Yokouchi, Yuki; Kakusaka, Mayumi; Hasegawa, Michihiro; Asai, Fumitoshi
CORPORATE SOURCE: Sankyo Co Ltd, Pharmacol and Mol Biol Res Labs, Tokyo, Japan
SOURCE: Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 534A. Meeting Info.: 47th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA. December 10 -13, 2005. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Mar 2006
Last Updated on STN: 15 Mar 2006

ABSTRACT:The thienopyridine antiplatelet prodrug clopidogrel bisulfate (C) is widely used for atherothrombotic diseases. However, several reports have described a limitation of C, namely poor platelet inhibition in many patients following oral dosing. Prasugrel (hydrochloride): currently under investigation in a Phase 3 trial in acute **coronary** syndrome patients undergoing **percutaneous coronary** intervention, is a novel thienopyridine antiplatelet prodrug. In recent clinical studies, prasugrel has

shown more consistent platelet inhibition than C. To date, several preclinical studies have demonstrated that the prasugrel base formulation has more potent antiplatelet and antithrombotic effects than C. The effects of prasugrel hydrochloride (P), which has a higher solubility than the base formulation, have not been reported. The present studies examined the effects of P on platelet aggregation, arterial thrombosis, and bleeding time in rats. Single oral administration of P (0.3 to 3 mg/kg) resulted in inhibition of platelet aggregation (IPA) induced by ADP in a dose- and time-related manner with an ED50 value of 1.1 mg/kg at 4 hr postdose. After dosing of 3 and 10 mg/kg P, statistically significant IPA was observed at 30 and 15 min, and the time required to achieve 50% IPA was approximately 50 and 23 min, respectively (Figure). These results indicate that P has potent antiplatelet effects with an extremely fast onset of action. Multiple P dosing also resulted in potent IPA, with an ED50 value of 0.45 mg/kg/day (p.o.) at 4 hr after the last dose. Our previous report indicated an ED50 value of C at 4 hr after single oral dosing of 16 mg/kg (Br. J. Pharmacol. 129, 1439, 2000), demonstrating about 10-times greater potency of P compared to C. Potent dose-related antithrombotic effects of P were further confirmed in an arterial thrombosis model in rats. P (0.1-1 mg/kg, p.o.) inhibited thrombus formation in the arterial thrombosis induced by extravascular application of FeCl3 solution. All these results taken together indicate that prasugrel hydrochloride is a novel, potent and fast acting thienopyridine prodrug, potentially providing superior efficacy in the treatment of atherothrombotic disorders.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Blood and hematopoietic agents 22008
Pharmacology - Cardiovascular system 22010
Toxicology - General and methods 22501
Immunology - General and methods 34502

INDEX TERMS: Major Concepts
Pharmacology; Cardiovascular System (Transport and Circulation); Immune System (Chemical Coordination and Homeostasis); Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics

INDEX TERMS: Diseases
arterial thrombosis: vascular disease, drug therapy, chemically-induced
Thrombosis (MeSH)

INDEX TERMS: Chemicals & Biochemicals
ADP; ferric chloride: toxin; clopidogrel bisulfate: anticoagulant-drug, hematologic-drug; prasugrel hydrochloride [CS-747, LY640315]: cardiovascular-drug, antithrombotic-drug, hematologic-drug, anticoagulant-drug, dosage, potency, preclinical trial, efficacy, oral administration

INDEX TERMS: Miscellaneous Descriptors
bleeding time; platelet aggregation inhibition

REGISTRY NUMBER: 175832-20-9 (ADP)
7705-08-0 (ferric chloride)
120202-66-6 (clopidogrel bisulfate)

Searched by Barb O'Bryen, STIC 2-2518

L16 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:13245 BIOSIS
DOCUMENT NUMBER: PREV199698585380
TITLE: Suppression of intracoronary thrombin activity by weight-adjusted heparin administration during coronary interventions.
AUTHOR(S): Snitzer, Robert; Hiremath, Yoganand J.; Lee, Joan; Lasala, John M.; Eisenberg, Paul R.; **Winters, Kenneth J.**
CORPORATE SOURCE: Washington Univ., St. Louis, MO, USA
SOURCE: Circulation, (1995) Vol. 92, No. 8 SUPPL., pp. I609.
Meeting Info.: 68th Scientific Session of the American Heart Association. Anaheim, California, USA. November 13-16, 1995.
CODEN: CIRCAZ. ISSN: 0009-7322.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jan 1996
Last Updated on STN: 4 Jan 1996
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Metabolism - Proteins, peptides and amino acids 13012
Cardiovascular system - Physiology and biochemistry 14504
Blood - Blood and lymph studies 15002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Cardiovascular System (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Pharmacology
INDEX TERMS: Chemicals & Biochemicals
THROMBIN; HEPARIN
INDEX TERMS: Miscellaneous Descriptors
ACTIVATED CLOTTING TIME; ANTICOAGULANT-DRUG; DIRECTIONAL CORONARY ATHERECTOMY; HEPARIN; MEETING ABSTRACT; **PERCUTANEOUS** TRANSLUMINAL **CORONARY** ANGIOPLASTY; THERAPY
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
REGISTRY NUMBER: 9002-04-4 (THROMBIN)
9005-49-6 (HEPARIN)

L16 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:13242 BIOSIS
DOCUMENT NUMBER: PREV199698585377

TITLE: Heparin-resistant thrombin activity is associated with acute ischemic events during high-risk coronary interventions.

AUTHOR(S): **Winters, Kenneth J.** [Reprint author]; Oltrona, Luigi; Hiremath, Yoganand J. [Reprint author]; Lasala, John M. [Reprint author]; Eisenberg, Paul R. [Reprint author]

CORPORATE SOURCE: Washington Univ., St. Louis, MO, USA

SOURCE: Circulation, (1995) Vol. 92, No. 8 SUPPL., pp. I608.
Meeting Info.: 68th Scientific Session of the American Heart Association. Anaheim, California, USA. November 13-16, 1995.
CODEN: CIRCAZ. ISSN: 0009-7322.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 4 Jan 1996
Last Updated on STN: 4 Jan 1996

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Metabolism - Proteins, peptides and amino acids 13012
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences); Metabolism; Pharmacology

INDEX TERMS: Chemicals & Biochemicals
HEPARIN; THROMBIN

INDEX TERMS: Miscellaneous Descriptors
ANTICOAGULANT-DRUG; CORONARY REVASCULARIZATION; HEPARIN; MEETING ABSTRACT; **PERCUTANEOUS** TRANSLUMINAL **CORONARY** ANGIOPLASTY; THROMBOSIS

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 9005-49-6 (HEPARIN)
9002-04-4 (THROMBIN)

L16 ANSWER 11 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:10516 BIOSIS

Searched by Barb O'Bryen, STIC 2-2518

DOCUMENT NUMBER: PREV199698582651
TITLE: Thrombin inhibition by novel arginal tripeptide LY296516 fails to inhibit intimal thickening in a rabbit model of arterial injury.
AUTHOR(S): Dube, Gregory P.; Kurtz, William L.; Brune, Kellie A.; Shuman, Robert T.; **Jakubowski, Joseph A.**; Craft, Trelia J.; Coffman, William J.; Smith, Gerald F.
CORPORATE SOURCE: Eli Lilly Co., Indianapolis, IN, USA
SOURCE: Circulation, (1995) Vol. 92, No. 8 SUPPL., pp. I35. Meeting Info.: 68th Scientific Session of the American Heart Association. Anaheim, California, USA. November 13-16, 1995.
CODEN: CIRCAZ. ISSN: 0009-7322.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jan 1996
Last Updated on STN: 4 Jan 1996
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Cardiovascular system - General and methods 14501
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Cardiovascular System (Transport and Circulation)
INDEX TERMS: Chemicals & Biochemicals
THROMBIN
INDEX TERMS: Miscellaneous Descriptors
MEETING ABSTRACT; **PERCUTANEOUS** TRANSLUMINAL **CORONARY** ANGIOPLASTY; RESTENOSIS
ORGANISM: Classifier
Leporidae 86040
Super Taxa
Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
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Taxa Notes
Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
REGISTRY NUMBER: 9002-04-4 (THROMBIN)

L16 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:202100 BIOSIS
DOCUMENT NUMBER: PREV199497215100
TITLE: Adaptation of myocardial ischemia to repetitive prolonged coronary occlusion in PTCA: Clinical, ECG, echocardiographic and metabolic assessment.
AUTHOR(S): Cribier, Alain; Eltchaninoff, Helene; Tron, Christophe; Koning, Rene; Derumeaux, Genevieve; Baala, Brahim; **Farid, Nasser**; Hecketsweiller, Bernadette; Letac, Brice
CORPORATE SOURCE: Hopital Charles Nicolle, Univ. Rouen, France
SOURCE: Journal of the American College of Cardiology, (1994) Vol. 0, No. SPEC. ISSUE, pp. 80A.

Meeting Info.: 43rd Annual Scientific Session of the American College of Cardiology. Atlanta, Georgia, USA. March 13-17, 1994.
CODEN: JACCDI. ISSN: 0735-1097.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 1994
Last Updated on STN: 2 May 1994
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Anatomy and Histology - Surgery 11105
Anatomy and Histology - Radiologic anatomy 11106
Pathology - Therapy 12512
Metabolism - General metabolism and metabolic pathways 13002
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508
Muscle - Pathology 17506
INDEX TERMS: Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Metabolism; Morphology; Muscular System (Movement and Support); Surgery (Medical Sciences)
INDEX TERMS: Miscellaneous Descriptors
CHRONIC ISCHEMIA; ELECTROCARDIOGRAPHY; MEETING ABSTRACT; **PERCUTANEOUS** TRANSLUMINAL **CORONARY** ANGIOPLASTY
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L16 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:494346 BIOSIS
DOCUMENT NUMBER: PREV199345105571
TITLE: Angioscopic evaluation of the immediate results of PTCA using prolonged sequential balloon inflations: A comparison with standard inflations.
AUTHOR(S): Eltchaninoff, H.; Cribier, A.; Koning, R.; Chan, C.; Baala, C.; **Farid, N.**; Jolly, N.; Saoudi, N.; Mechmeche, R.; Letac, B.
CORPORATE SOURCE: Hop C. Nicolle Voacomed, Univ. Rouen, Rouen, France
SOURCE: European Heart Journal, (1993) Vol. 14, No. ABSTR. SUPPL., pp. 475.
Meeting Info.: XVth Congress of the European Society of Cardiology. Nice, France. August 29-September 2, 1993.
CODEN: EHJODF. ISSN: 0195-668X.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Oct 1993
Last Updated on STN: 28 Oct 1993
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520

Searched by Barb O'Bryen, STIC 2-2518

Radiation biology - Radiation and isotope techniques 06504
Biophysics - Methods and techniques 10504
Anatomy and Histology - Surgery 11105
Anatomy and Histology - Radiologic anatomy 11106
Pathology - Therapy 12512
Cardiovascular system - General and methods 14501
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508

INDEX TERMS: Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Cardiovascular System (Transport and Circulation); Radiology (Medical Sciences)

INDEX TERMS: Miscellaneous Descriptors
ABSTRACT; ANALYTICAL METHOD; LUMINAL STENOSIS; MYOCARDIAL INFARCTION; **PERCUTANEOUS** TRANSLUMINAL **CORONARY** ANGIOPLASTY

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

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=> fil reg; d ide l7
FILE 'REGISTRY' ENTERED AT 11:22:50 ON 10 AUG 2006
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DICTIONARY FILE UPDATES:   9 AUG 2006  HIGHEST RN 900096-56-2

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predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html


L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   150322-43-3  REGISTRY
ED   Entered STN:  29 Sep 1993
CN   Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-
     cyclopropyl-2-(2-fluorophenyl)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Thieno[3,2-c]pyridine, ethanone deriv.
OTHER NAMES:
CN   CS 747
CN   Prasugrel
FS   3D CONCORD
MF   C20 H20 F N O3 S
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, BIOSIS, CA, CAPLUS, CIN, IMSDRUGNEWS,
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       USAN, USPAT2, USPATFULL
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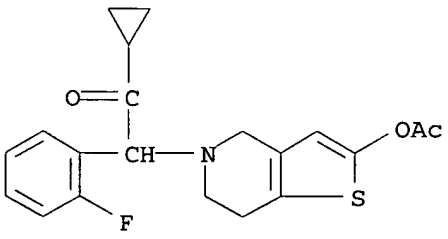

Formula I

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
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Searched by Barb O'Bryen, STIC 2-2518

26 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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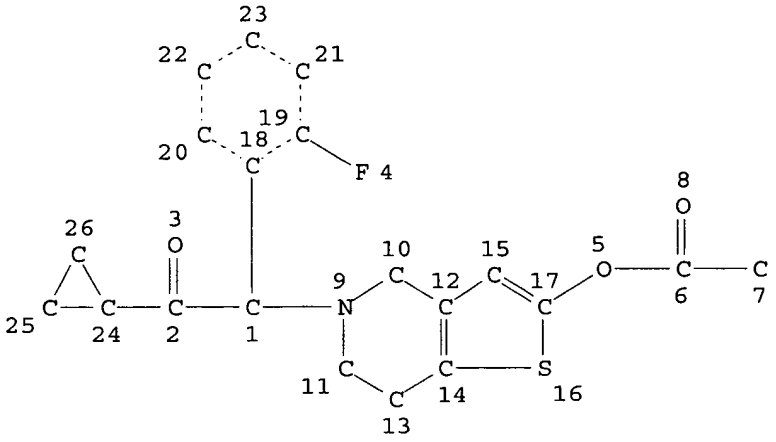
L17 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L19 3 SEA FILE=REGISTRY FAM FUL L17

100.0% PROCESSED 14 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

=> d ide l19 1-3; fil capl; d que nos l20; s l20 not l5; fil embase; d que nos l33
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:=> d ide l19 1-3;
fil capl; d que nos l20; s l20 not l5; fil embase; d que nos l33

L19 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 389574-20-3 REGISTRY
ED Entered STN: 05 Feb 2002
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H20 F N O3 S . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

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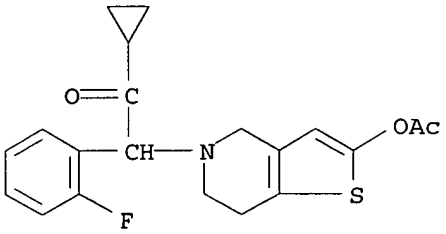
CRN 150322-43-3
CMF C20 H20 F N O3 S



CM 2

CRN 110-16-7
CMF C4 H4 O4

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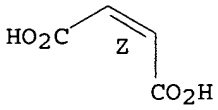
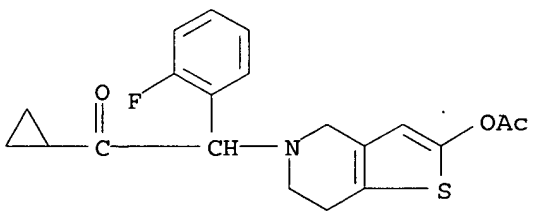


4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 389574-19-0 REGISTRY
ED Entered STN: 05 Feb 2002
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, hydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN LY 640315
CN Prasugrel hydrochloride
MF C20 H20 F N O3 S . Cl H
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, EMBASE, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
CRN (150322-43-3)



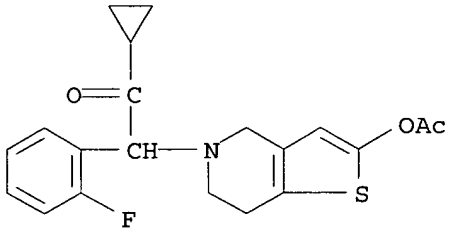
compound of claim 5

● HCl

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Searched by Barb O'Bryen, STIC 2-2518

L19 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 150322-43-3 REGISTRY
ED Entered STN: 29 Sep 1993
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Thieno[3,2-c]pyridine, ethanone deriv.
OTHER NAMES:
CN CS 747
CN Prasugrel
FS 3D CONCORD
MF C20 H20 F N O3 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, CA, CAPLUS, CIN, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

26 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

FILE 'EMBASE' ENTERED AT 11:35:21 ON 10 AUG 2006

FILE COVERS 1974 TO 10 Aug 2006 (20060810/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L17 STR
L19 3 SEA FILE=REGISTRY FAM FUL L17
L25 34 SEA FILE=EMBASE ABB=ON L19
L26 1218793 SEA FILE=EMBASE ABB=ON CARDIOVASCULAR DISEASE+NT/CT
L27 14231 SEA FILE=EMBASE ABB=ON PCI OR PERCUTANEOUS?(5A)CORONARY
L28 13711 SEA FILE=EMBASE ABB=ON TRANSLUMINAL CORONARY ANGIOPLASTY/CT

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L30       82369 SEA FILE=EMBASE ABB=ON  ACETYLSALICYLIC ACID/CT
L31       27019 SEA FILE=EMBASE ABB=ON  STENT+NT/CT
L33          23 SEA FILE=EMBASE ABB=ON  L25 AND (L30 OR L31) AND (L26 OR L27
                OR L28)


=> fil ipa biosis toxcenter imsre prousddr; d que nos 123
FILE 'IPA' ENTERED AT 11:35:41 ON 10 AUG 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'BIOSIS' ENTERED AT 11:35:41 ON 10 AUG 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'TOXCENTER' ENTERED AT 11:35:41 ON 10 AUG 2006
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FILE 'IMSRESEARCH' ENTERED AT 11:35:41 ON 10 AUG 2006
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FILE 'PROUSDDR' ENTERED AT 11:35:41 ON 10 AUG 2006
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L17             STR
L19           3 SEA FILE=REGISTRY FAM FUL L17
L23          27 SEA L19


=> => fil wpix; d que l42
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COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE LAST UPDATED:          9 AUG 2006      <20060809/UP>
MOST RECENT DERWENT UPDATE:     200651        <200651/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS
    INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE


L37          11 SEA FILE=WPIX ABB=ON  RA7RM2/DCN OR 199852-0-0-0/DCRE OR
                PRASUGREL/BI,ABEX OR CS747/BI,ABEX OR CS 747/BI,ABEX
L39        4469 SEA FILE=WPIX ABB=ON  R00034/DCN OR R06663/DCN OR 87874-0-0-0/D
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                SALICYLIC/BI,ABEX
L40        8483 SEA FILE=WPIX ABB=ON  STENT#/BI,ABEX
L41        4848 SEA FILE=WPIX ABB=ON  PCI/BI,ABEX OR (PERCUTANEOUS?/BI,ABEX OR
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=> fil capl; d que nos l48; d que nos l51; s l48,l51 not l5
FILE 'CAPLUS' ENTERED AT 11:46:37 ON 10 AUG 2006
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L20          27 SEA FILE=CAPLUS ABB=ON  L19
L44           1 SEA FILE=REGISTRY ABB=ON  ASPIRIN/CN
L45       20321 SEA FILE=CAPLUS ABB=ON  L44
L46        4141 SEA FILE=CAPLUS ABB=ON  STENT#/OBI
L47        7059 SEA FILE=CAPLUS ABB=ON  (PCI OR (PERCUTANEOUS? OR PER CUTANEOUS
                ? OR TRANSLUMINAL? OR TRANS LUMINAL?)(5A)CORONARY)/BI
L48          12 SEA FILE=CAPLUS ABB=ON  L20 AND (L45 OR L46 OR L47)



L17             STR
L19           3 SEA FILE=REGISTRY FAM FUL L17
L20          27 SEA FILE=CAPLUS ABB=ON  L19
L51           1 SEA FILE=CAPLUS ABB=ON  L20 AND COATINGS/TI


L52          12 (L48 OR L51) NOT L5

=> dup rem l52,l23,l33,l42
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PROCESSING COMPLETED FOR L23
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L42
L53           56 DUP REM L52 L23 L33 L42 (15 DUPLICATES REMOVED)
                 ANSWERS '1-12' FROM FILE CAPLUS
                 ANSWERS '13-14' FROM FILE IPA
                 ANSWERS '15-23' FROM FILE BIOSIS
                 ANSWERS '24-28' FROM FILE TOXCENTER
                 ANSWER '29' FROM FILE IMSRESEARCH
                 ANSWER '30' FROM FILE PROUSDDR
                 ANSWERS '31-53' FROM FILE EMBASE
                 ANSWERS '54-56' FROM FILE WPIX

=> d ibib ed abs hitstr 1-12; d iall 13-53; d iall abeq tech 54-56; fil hom

L53  ANSWER 1 OF 56  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:170095  CAPLUS
DOCUMENT NUMBER:          144:226296
TITLE:                    Oral prophylactic agents for thrombosis and embolism
INVENTOR(S):              Morishima, Yoshiyuki; Watanabe, Kengo
PATENT ASSIGNEE(S):       Daiichi Seiyaku Co., Ltd., Japan
SOURCE:                   Jpn. Kokai Tokkyo Koho, 29 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     JP 2006052208         A2    20060223    JP 2005-202010           20050711
PRIORITY APPLN. INFO.:                       JP 2004-205486       A   20040713
OTHER SOURCE(S):          MARPAT 144:226296
ED   Entered STN:  24 Feb 2006
GI
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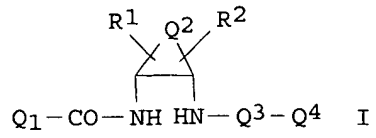

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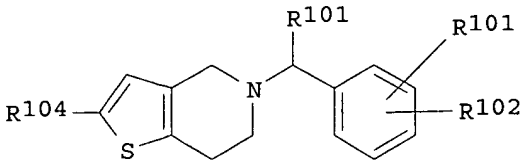

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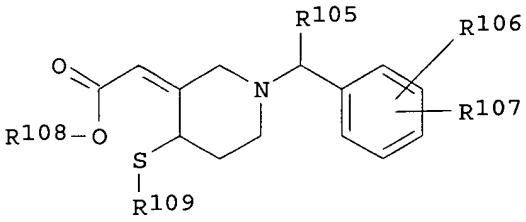


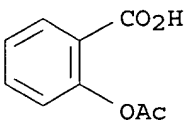
III

AB Title agents contain diamines I [Q1 = (un)substituted 4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl, 4,5,6,7-tetrahydrothiazolo[4,5-c]pyridin-2-yl, 4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl, 4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl, 4,6-dihydro-5H-pyrrolo[3,4-d]thiazol-2-yl, etc.; Q2 = C1-8 alkylene, (CH2)pA(CH2)q (p, q = 1-3; p + q = 2-4); A = O, N, S, SO, SO2, NH; R1, R2 = H, OH, NH2, CO2H, (halo)alkyl, acyl, alkoxycarbonylalkyl, (un)substituted acylamino, (un)substituted 3- to 6-membered heterocyclylcarbonyl, etc.; Q3 = CO, SO2, COCONH, CSCONH, COCSNH, CSCSNH; Q4 = (un)substituted Ph, naphthyl, pyridyl, pyrimidyl, indolyl, benzothienyl, furyl, etc.] and antiplatelet agents chosen from aspirin, sarpogrelate, limaprost, cilostazol, and piperidines II or III [R101, R105 = H, lower alkyl, lower alkoxycarbonyl, lower alkylcarbonyl; R102, R103, R106, R107 = H, lower alkyl, halo; R104 = H, OH, lower alkylcarbonyloxy; R108 = H, lower alkyl; R109 = H, lower alkylcarbonyl] as active ingredients. Thus, combination use of N1-(5-chloropyridin-2-yl)-N2-[(1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-[[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino]cyclohexyl]ethanediamide HCl salt (IV) and ticlopidine prevented 75% thrombosis formation in rats. CYP2D6- and CYP3A4-dependent metabolism of IV was 0.1-0.81 pmol/pmol/CYP/min, suggesting nonsusceptibility of IV to the enzymes.

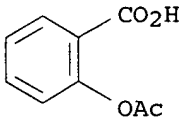
IT **50-78-2**, Aspirin **50-78-2D**, Aspirin, mixts. containing **150322-43-3 150322-43-3D**, mixts. containing
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination use of diamines and antiplatelet agents for oral prophylactic agents for thrombosis and embolism)

RN 50-78-2 CAPLUS

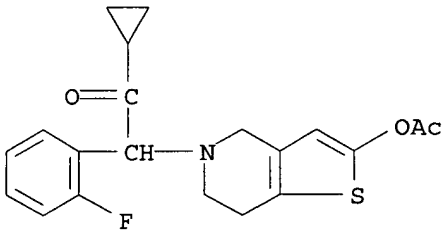
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



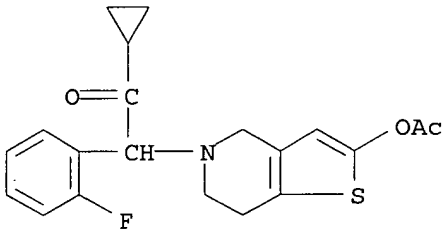
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



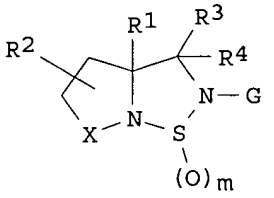
L53 ANSWER 2 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2005:902874 CAPLUS
DOCUMENT NUMBER: 143:248277
TITLE: Preparation of sulfonylpyrrolidines as modulators of androgen receptor
INVENTOR(S): Hamann, Lawrence H.; Bi, Yingzhi; Manfredi, Mark C.; Nirschl, Alexandra A.; Sutton, James C.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077925	A1	20050825	WO 2005-US2834	20050202

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-541869P P 20040204
OTHER SOURCE(S): MARPAT 143:248277
ED Entered STN: 26 Aug 2005

GI



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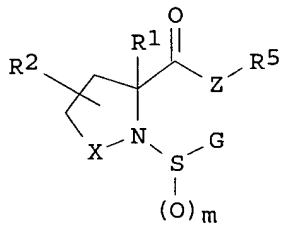

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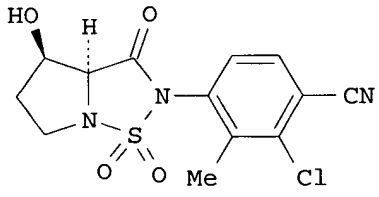
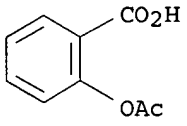


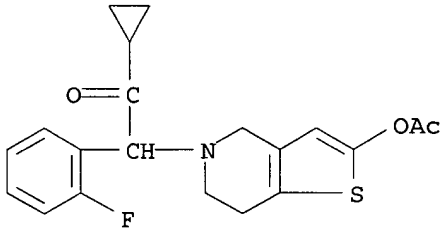
III

AB Title compds. I or II [R1 = H, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, SR6, etc.; R3 and R4 independently = H, (un)substituted alkynyl, cycloalkyl, etc.; R5 = H, (un)substituted aryl, arylalkyl, etc.; R6 = H, CHF2, CF3, etc.; X = (CH2)n; G = (un)substituted aryl, heterocycle or heteroaryl; Z = O or NR7; R7 = H, (un)substituted alkyl, alkenyl, etc.; n and m independently = 1-2] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of androgen receptor. Thus, e.g., III was prepared by hydrolysis of (2S,3R)-1-(3-chloro-4-cyano-2-methyl-phenylsulfamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid Me ester (preparation given) followed by cyclization. The activity of I was evaluated in transactivation assays of a transfected reporter construct and using the endogenous androgen receptor of the host cells (no data). I as modulator of androgen receptor should prove useful in the treatment of neoplasm, Alzheimer's disease and obesity. Pharmaceutical compns. comprising I are disclosed.

IT **50-78-2**, Aspirin **150322-43-3**, CS-747
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of sulfonylpyrrolidines as modulators of androgen receptor)
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



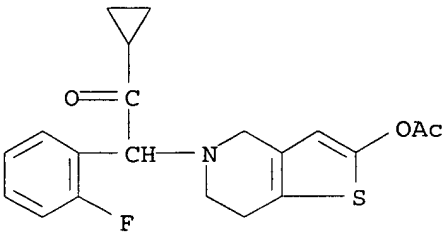
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 3 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2005:961492 CAPLUS
DOCUMENT NUMBER: 143:254076
TITLE: Drug eluting **coatings** for medical implants and methods of use
INVENTOR(S): Hsu, Li-Chien
PATENT ASSIGNEE(S): Biotegra, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S. Ser. No. 423,718.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005191333	A1	20050901	US 2005-119075		20050428
US 2004037886	A1	20040226	US 2003-423718		20030426
PRIORITY APPLN. INFO.:			US 2002-405933P	P	20020826
			US 2003-423718	A2	20030426

ED Entered STN: 02 Sep 2005
AB A drug coating for a medical device comprises one or more drug composite layers. The drug composite layer comprises one or more therapeutic agents dispersed within one or more modified bioactive binders. The modified bioactive binders are hydrophobic compds. bonded to bioactive binders, and the modified bioactive binders are not inert polymers.
IT **150322-43-3**, Prasugrel

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug eluting coatings for medical implants and methods of use)
RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 4 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2005:904349 CAPLUS
DOCUMENT NUMBER: 143:248278
TITLE: Preparation of sulfonylpyrrolidines as modulators of androgen receptor
INVENTOR(S): Hamann, Lawrence G.; Bi, Yingzhi; Manfredi, Mark C.; Nirschl, Alexandra A.; Sutton, James C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 35 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187267	A1	20050825	US 2005-48439	20050201
PRIORITY APPLN. INFO.:			US 2004-541869P P	20040204

OTHER SOURCE(S): MARPAT 143:248278
ED Entered STN: 26 Aug 2005
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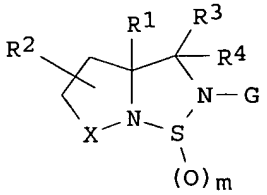

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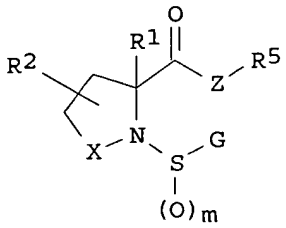

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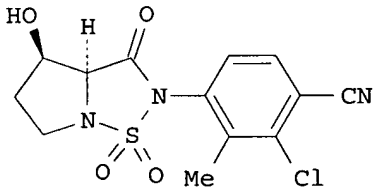
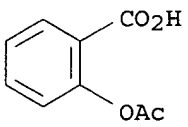


III

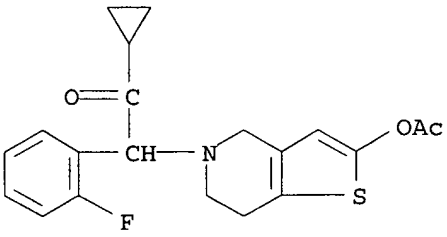
AB Title compds. I or II [R1 = H, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, SR6, etc.; R3 and R4 independently = H, (un)substituted alkynyl, cycloalkyl, etc.; R5 = H, (un)substituted aryl, arylalkyl, etc.; R6 = H, CHF2, CF3, etc.; X = (CH2)n; G = (un)substituted aryl, heterocycle or heteroaryl; Z = O or NR7; R7 = H, (un)substituted alkyl, alkenyl, etc.; n and m independently = 1-2] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of androgen receptor. Thus, e.g., III was prepared by hydrolysis of (2S,3R)-1-(3-chloro-4-cyano-2-methyl-phenylsulfamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid Me ester (preparation given) followed by cyclization. The activity of I was evaluated in transactivation assays of a transfected reporter construct and using the endogenous androgen receptor of the host cells (no data). I as modulator of androgen receptor should prove useful in the treatment of neoplasm, Alzheimer's disease and obesity. Pharmaceutical compns. comprising I are disclosed.

IT **50-78-2 150322-43-3**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of sulfonylpyrrolidines as modulators of androgen receptor)

RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



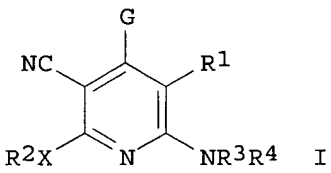
RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 5 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2005:824492 CAPLUS
DOCUMENT NUMBER: 143:222525
TITLE: Method of using 3-cyano-4-arylpyridine derivatives as modulators of androgen receptor function, preparation thereof, and use with other agents
INVENTOR(S): Nirschl, Alexandra A.; Hamann, Lawrence G.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005182105	A1	20050818	US 2005-48437	20050201
PRIORITY APPLN. INFO.:			US 2004-541780P P	20040204

OTHER SOURCE(S): MARPAT 143:222525
ED Entered STN: 19 Aug 2005
GI



AB A method is provided for treating androgen receptor-associated conditions, such as age-related diseases, e.g. sarcopenia, employing a compound I [R1 = CN, H; X = O, S; R2 = (substituted) alkyl, (substituted) cycloalkyl, etc; R3, R4 = H, (substituted) alkyl, etc.; G = (substituted) aryl, (substituted) heteroaryl], or a pharmaceutically acceptable salt or prodrug ester thereof. Preparation of selected I is described. I may be used in combination with other agents.

IT **50-78-2**, Aspirin **150322-43-3**, CS-747
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyanoarylpyridine derivative modulators of androgen receptor function, preparation, and use with other agents)

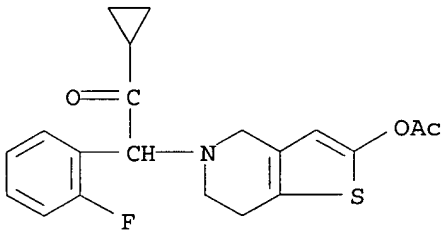
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)

(TIMI major plus minor) non-CABG-related bleeding events in prasugrel- vs. clopidogrel-treated patients. Hemorrhagic complications were infrequent, with no significant difference between patients treated with prasugrel or clopidogrel in the rate of significant bleeding (1.7% vs. 1.2%; hazard ratio, 1.42; 95% CI, 0.40, 5.08). In prasugrel-treated patients, there were numerically lower incidences of the primary efficacy composite end point (30-day major adverse cardiac events) and of the secondary end points myocardial infarction, recurrent ischemia, and clin. target vessel thrombosis. Conclusions: In this phase 2 study, which was designed to assess safety when administered at the time of **percutaneous coronary** intervention, prasugrel and clopidogrel both resulted in low rates of bleeding. The results of this trial serve as a foundation for the large phase 3 clin. trial designed to assess both efficacy and safety.

IT **150322-43-3**, Prasugrel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LY640315; prasugrel and clopidogrel both were safe, effective and resulted in low rates of bleeding in patient after **percutaneous coronary** intervention)

RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



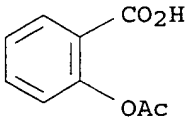
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 7 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

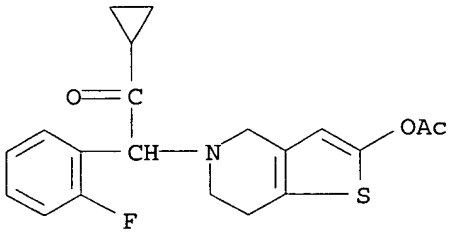
ACCESSION NUMBER: 2005:480490 CAPLUS
DOCUMENT NUMBER: 143:205548
TITLE: Pharmacology of CS-747 (prasugrel, LY640315), a novel, potent antiplatelet agent with in vivo P2Y12 receptor antagonist activity
AUTHOR(S): Niitsu, Yoichi; Jakubowski, Joseph A.; Sugidachi, Atsuhiro; Asai, Fumitoshi
CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Sankyo Co., Ltd., Tokyo, Japan
SOURCE: Seminars in Thrombosis and Hemostasis (2005), 31(2), 184-194
CODEN: STHMBV; ISSN: 0094-6176
PUBLISHER: Thieme Medical Publishers, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

ED Entered STN: 07 Jun 2005

AB A review. CS-747 (prasugrel, LY640315) is a member of the thienopyridine class of oral platelet aggregation inhibitors that includes ticlopidine and clopidogrel. A single oral administration of CS-747 produced a dose-related inhibition of platelet aggregation in rats that was approx. 10- and 100-fold more potent than that of clopidogrel and ticlopidine,



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)

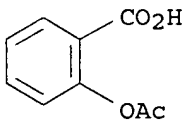


L53 ANSWER 6 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2005:548016 CAPLUS
DOCUMENT NUMBER: 143:359712
TITLE: Randomized Comparison of Prasugrel (CS-747, LY640315), a Novel Thienopyridine P2Y12 Antagonist, with Clopidogrel in **Percutaneous Coronary** Intervention
AUTHOR(S): Wiviott, Stephen D.; Antman, Elliott M.; Winters, Kenneth J.; Weerakkody, Govinda; Murphy, Sabina A.; Behounek, Bruce D.; Carney, Robert J.; Lazzam, Charles; McKay, Raymond G.; McCabe, Carolyn H.; Braunwald, Eugene
CORPORATE SOURCE: the JUMBO-TIMI 26 Investigators, TIMI Study Group, Cardiovascular Division, Brigham and Women's Hospital, Department of Medicine, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Circulation (2005), 111(25), 3366-3373
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Jun 2005
AB Background: Despite the current standard antiplatelet regimen of aspirin and clopidogrel (with or without glycoprotein IIb/IIIa inhibitors) in **percutaneous coronary** intervention patients, periprocedural and postprocedural ischemic events continue to occur. Prasugrel (CS-747, LY640315), a novel potent thienopyridine P2Y12 receptor antagonist, has the potential to achieve higher levels of inhibition of ADP-induced platelet aggregation than currently approved doses of clopidogrel. Methods and Results: Joint Utilization of Medications to Block Platelets Optimally-Thrombolysis In Myocardial Infarction 26 (JUMBO-TIMI 26) was a phase 2, randomized, dose-ranging, double-blind safety trial of prasugrel vs. clopidogrel in 904 patients undergoing elective or urgent **percutaneous coronary** intervention. Patients were randomized to either standard dosing with clopidogrel or 1 of 3 prasugrel regimens. Subjects were monitored for 30 days for bleeding and clin. events. The primary end point of the trial was clin. significant

L53 ANSWER 8 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 2002:813926 CAPLUS
DOCUMENT NUMBER: 137:304829
TITLE: Enantiomers of N-[[2'-[[(4,5-dimethyl-3-isoxazolyl) amino]sulfonyl]-4-(2-oxazolyl)[1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethylbutanamide
INVENTOR(S): Hughes, David E.; Seidenberg, Beth C.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083130	A1	20021024	WO 2002-US11992	20020412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003040534	A1	20030227	US 2002-121520	20020412
PRIORITY APPLN. INFO.:			US 2001-284080P P	20010416

ED Entered STN: 25 Oct 2002
AB Endothelin antagonist N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino] sulfonyl]-4-(2-oxazolyl)[1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethylbutanamide surprisingly exists as separable enantiomeric atropisomers. The (+)-dextrorotatory atropisomer demonstrates remarkably higher potency than either the (-)-levorotatory atropisomer or the racemate. The (+)-dextrorotatory atropisomer is suitable for treatment of endothelin-related disorders, such as hypertension, renal diseases, atherosclerosis, restenosis, congestive heart failure, diabetic nephropathy, cancer, asthma, etc., alone or in combination with, e.g., angiotensin, renin, or ACE inhibitors, diuretics, cardiac glycosides, antiplatelet agents, etc.
IT **50-78-2**, Aspirin **150322-43-3**, CS 747
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; therapeutic uses of enantiomers of biphenyl isoxazole sulfonamide derivative as endothelin antagonists)
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



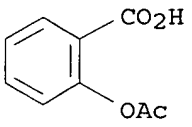
RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)

resp. The antiaggregatory effect of CS-747 was evident at 30 min and lasted until 72 h after dosing, indicating fast onset and long duration of action. CS-747 showed more potent antithrombotic activity compared with clopidogrel and ticlopidine with the same rank order as the antiaggregatory potencies. Combined administration of CS-747 with aspirin to rats produced substantially greater inhibition of both platelet aggregation and thrombus formation compared with each agent alone. The antiplatelet action of CS-747 is due to irreversible and selective blockade of platelet P2Y12 ADP (ADP) receptors by its active metabolite R-138727. In phase I studies, a single oral dose of CS-747 (30 and 75 mg) produced > 50% inhibition of ADP-induced platelet aggregation, with rapid onset (1 h) and long duration (>48 h) of action. In healthy volunteers, once-daily administration of 10 mg CS-747 for 10 days showed significant cumulative inhibition of platelet aggregation from 2 days after the first dose until at least 2 days after the final dose. Studies conducted to date indicate that CS-747 is a highly effective antiplatelet and antithrombotic agent and is anticipated to be effective in the treatment of atherothrombotic and other ischemic vascular diseases.

IT **50-78-2**, Aspirin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CS-747 alone or in combination with aspirin exhibited more potent antiplatelet activity and antithrombotic activity than ticlopidine and clopidogrel indicating that CS-747 may be effective in treatment of atherothrombotic disease patient)

RN 50-78-2 CAPLUS

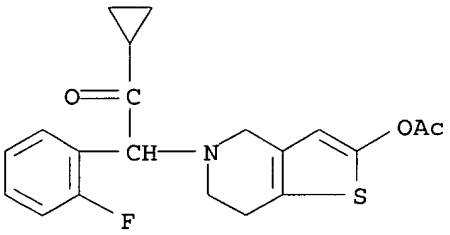
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



IT **150322-43-3**, CS 747
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LY640315 alone or with aspirin exhibited more potent antiplatelet activity and antithrombotic activity than ticlopidine and clopidogrel indicating that CS-747 may be effective in treatment of patient with atherothrombotic disease)

RN 150322-43-3 CAPLUS

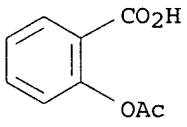
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



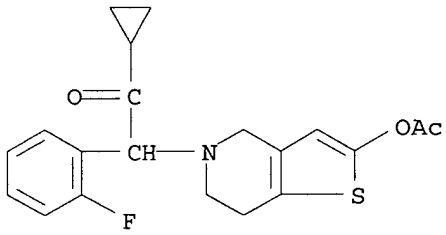
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicinal compns. containing aspirin and thienopyridinylethanone derivative)

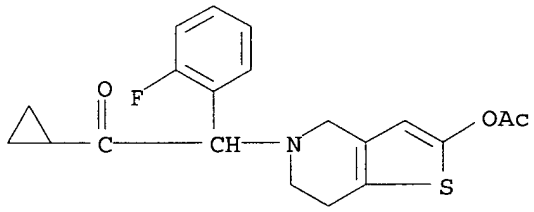
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 389574-19-0 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, hydrochloride (9CI) (CA INDEX NAME)

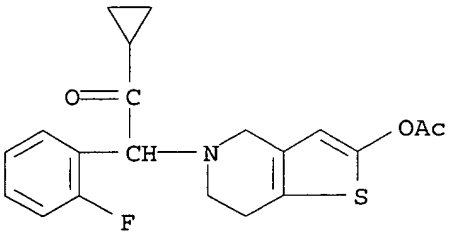


● HCl

RN 389574-20-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 150322-43-3
CMF C20 H20 F N O3 S



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

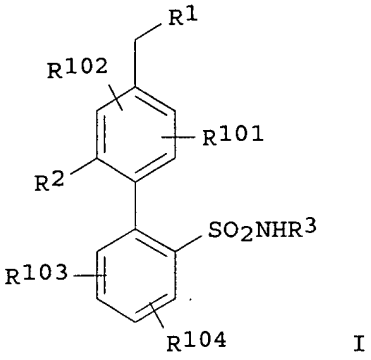
L53 ANSWER 9 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 2002:504621 CAPLUS
DOCUMENT NUMBER: 137:52422
TITLE: Medicinal compositions containing aspirin
INVENTOR(S): Asai, Fumitoshi; Sugidachi, Atsuhiro; Ogawa, Taketoshi; Inoue, Teruhiko
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan; Ube Industries, Ltd.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051412	A1	20020704	WO 2001-JP11201	20011220
W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PH, PL, RU, SG, SK, US, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2432644	AA	20020704	CA 2001-2432644	20011220
JP 2002255814	A2	20020911	JP 2001-386850	20011220
EP 1350511	A1	20031008	EP 2001-271850	20011220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
BR 2001016531	A	20040225	BR 2001-16531	20011220
CN 1491109	A	20040421	CN 2001-822768	20011220
NZ 526540	A	20041126	NZ 2001-526540	20011220
RU 2262933	C2	20051027	RU 2003-118638	20011220
US 2004024013	A1	20040205	US 2003-600266	20030620
ZA 2003004878	A	20040810	ZA 2003-4878	20030623
NO 2003002902	A	20030624	NO 2003-2902	20030624
PRIORITY APPLN. INFO.:			JP 2000-392983 A	20001225
			WO 2001-JP11201 W	20011220

ED Entered STN: 05 Jul 2002
AB Disclosed are medicinal compns. containing as the active ingredients 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2 c]pyridine (I) or its pharmacol. acceptable salt and aspirin. Because of having excellent inhibitory effects on platelet aggregation and thrombosis, these compns. are useful as preventives or remedies for diseases induced by thrombus or embolization. A tablet was formulated containing I 10, aspirin 12.5, lactose 175.5, starch 50, and Mg stearate 2 mg.
IT **50-78-2**, Aspirin **150322-43-3 389574-19-0 389574-20-3**

US 2000-737201 A3 20001214

OTHER SOURCE(S): MARPAT 137:263024
ED Entered STN: 04 Oct 2002
GI

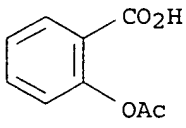


I

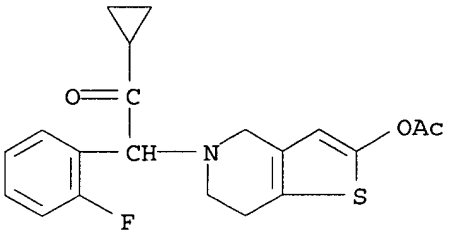
AB Title compds. (I; R1 = specified oxoimidazolyl, pyridoimidazolyl, pyridylamino, pyridyloxy, triazolyl, quinolinyloxy, etc.; R2 = H, halo, CHO, (halo)alkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxy, cyano, OH, NO2, etc.; R3 = heteroaryl; R101-R104 = H, halo, CHO, alkyl, haloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, alkoxyalkoxy, cyano, OH, hydroxyalkyl, NO2, etc; with provisos) were prepared as dual angiotensin II and endothelin receptor antagonists for treatment of hypertension and other diseases (no data). Thus, 4-BrC6H4CH2OH was coupled with [2-[[(4,5-dimethyl-3-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl]phenyl]boronic acid to give N-(4,5-dimethyl-3-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl][1,1'-biphenyl]-2-sulfonamide (66%). This was brominated to give the 4'-bromomethyl derivative (90%), reacted with 2-butyl-1,3-diazaspiro[4.4]non-1-en-4-one hydrochloride, and deprotected (49% for two steps) to give 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-[1,1'-biphenyl]-2-sulfonamide.

IT **50-78-2**, Aspirin **150322-43-3**, Cs-747
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



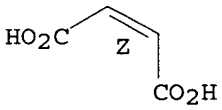
RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



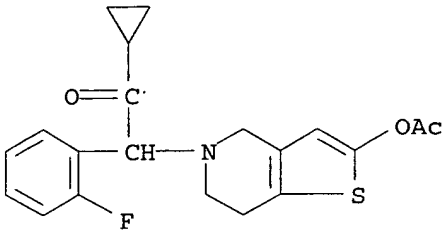
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 10 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 2002:755214 CAPLUS
DOCUMENT NUMBER: 137:263024
TITLE: Preparation of N-isoxazolyl biphenylsulfonamides and related compounds as dual angiotensin II and endothelin receptor antagonists.
INVENTOR(S): Murugesan, Natesan; Tellew, John E.; Macor, Jhon E.; Gu, Zhengxiang
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: U.S. Pat. Appl. Publ., 206 pp., Cont.-in-part of U.S. Ser. No. 643,640, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002143024	A1	20021003	US 2000-737201	20001214
US 6638937	B2	20031028		
US 2004106833	A1	20040603	US 2003-673100	20030926
US 6835741	B2	20041228		
US 2004127515	A1	20040701	US 2003-672572	20030926
US 6852745	B2	20050208		

PRIORITY APPLN. INFO.:

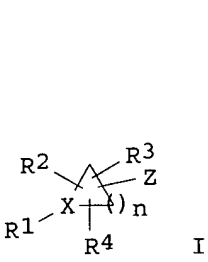
US 1998-91847P	P	19980706
US 1999-345392	B2	19990701
US 1999-464037	B2	19991215
US 2000-481197	B2	20000111
US 2000-513779	A2	20000225
US 2000-604322	A2	20000626
US 2000-643640	B2	20000822



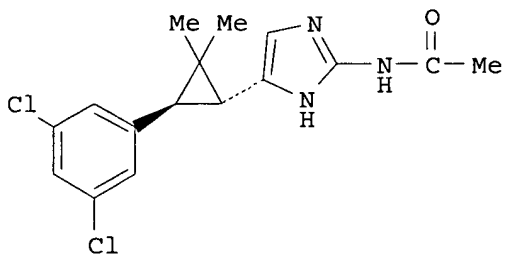
L53 ANSWER 11 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12
ACCESSION NUMBER: 2001:283949 CAPLUS
DOCUMENT NUMBER: 134:311218
TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors
INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001027107	A2	20010419	WO 2000-US27461		20001002
WO 2001027107	A3	20020124			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6887870	B1	20050503	US 2000-669298		20000925
CA 2388813	AA	20010419	CA 2000-2388813		20001002
EP 1224183	A2	20020724	EP 2000-968723		20001002
EP 1224183	B1	20051228			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
BR 2000014725	A	20030617	BR 2000-14725		20001002
JP 2003527331	T2	20030916	JP 2001-530325		20001002
NZ 517668	A	20040924	NZ 2000-517668		20001002
AT 314364	E	20060115	AT 2000-968723		20001002
ES 2254236	T3	20060616	ES 2000-968723		20001002
ZA 2002002479	A	20040727	ZA 2002-2479		20020327
NO 2002001717	A	20020610	NO 2002-1717		20020411
US 2005137216	A1	20050623	US 2005-46993		20050131
PRIORITY APPLN. INFO.:			US 1999-158755P	P	19991012
			US 2000-669298	A3	20000925
			WO 2000-US27461	W	20001002

OTHER SOURCE(S): MARPAT 134:311218
ED Entered STN: 20 Apr 2001
GI



I

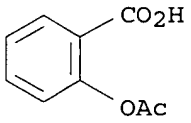


II

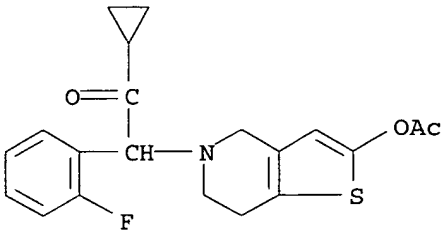
AB Compds. of formula I [wherein; n is 1-5; X is N or CR5, where R5 is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R1 is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R2, R3 and R4 are any of the groups set out for R1 and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R1 is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding α-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, β-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT **50-78-2**, Aspirin **150322-43-3**, CS 747
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals also containing; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



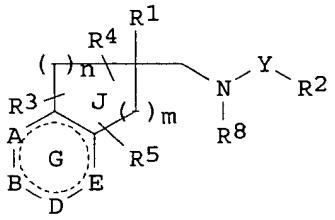
RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



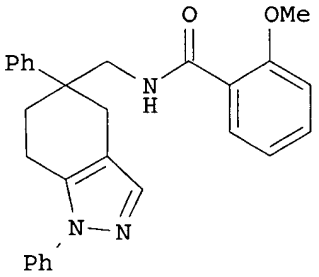
L53 ANSWER 12 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1200967 CAPLUS
DOCUMENT NUMBER: 143:460154
TITLE: Preparation of fused heterocyclic compounds as potassium channel modulators
INVENTOR(S): Johnson, James A.; Lloyd, John; Kover, Alexander
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105096	A2	20051110	WO 2005-US12542	20050414
WO 2005105096	A3	20060706		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005250783	A1	20051110	US 2005-104856	20050413
PRIORITY APPLN. INFO.:			US 2004-563143P P	20040415

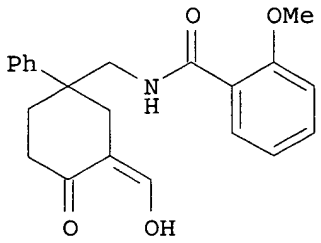
OTHER SOURCE(S): MARPAT 143:460154
ED Entered STN: 11 Nov 2005
GI



I



II

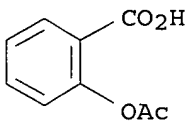


III

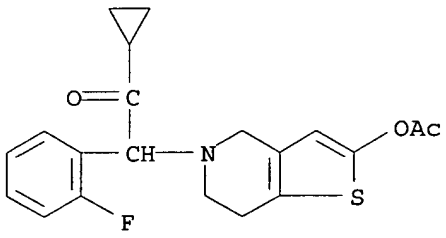
AB Compds. of formula I [n and m are integers such that ring J is a 5-7 membered ring; A, B, D, and E are -CR6=, -CR6-, -CO-, -NR7-, -N=, -O-, -S-, a bond or a double bond, such that ring G is a 5-6 membered heterocycle with at least one N atom; R1 = aryl substituted with one or more X; X = -(CH2)p(Z1)q(CH2)aZ2 which substituents may together form an (un)substituted carbocycle or heterocycle; R2 = aryl, heteroaryl, cycloalkyl or heterocyclo each optionally substituted with one or more X; Y = -CO-, -C(=S)-, -SO2, etc.; R3-8 are the same or different and independently equal to X, or R3-5 may in pairs of two form an (un)substituted carbocycle or heterocycle, or R6 and R7 together in pairs of two form an (un)substituted carbocycle or heterocycle, etc.; Z1 = S, SO, CO, etc.; Z2 = H, (un)substituted alkyl, alkenyl, etc.; p and a independently = 0-10; q = 0-1], and their pharmaceutically acceptable salts, are prepared and disclosed as potassium channel modulators (no data). Thus, e.g., II was prepared by cyclocondensation of III (preparation given) with Ph hydrazine. Pharmaceutical compns. are provided.

IT **50-78-2**, Aspirin **150322-43-3**, CS-747
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fused heterocyclic compds. and their use for treatment of diseases)

RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 13 OF 56 IPA COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 2006:8292 IPA
DOCUMENT NUMBER: 43-09792
TITLE: The platelet inhibitory effects and pharmacokinetics of prasugrel after administration of loading and maintenance doses in healthy subjects
AUTHOR: Jakubowski, JA; Payne, CD; Brandt, JT; Weerakkody, GJ; Winters, KJ; et al
CORPORATE SOURCE: Eli Lilly & Co, Lilly Corp Ctr, 6075, Indianapolis, IN 46285, USA joseph@lilly.com
SOURCE: Journal of Cardiovascular Pharmacology (USA), (2006) Vol. 47, pp. 377-384. 30 Refs.
CODEN: JCPCDT; ISSN: 0160-2446.
DOCUMENT TYPE: Journal
FILE SEGMENT: HUMAN
LANGUAGE: English
ABSTRACT:

The results of a double-blind, placebo-controlled, randomized, parallel group study evaluating the platelet inhibitory effects and pharmacokinetics of prasugrel (CS-747) after administration of loading and maintenance doses in healthy subjects (n=28) are presented.

The results from this combined loading dose and maintenance dose study in healthy subjects indicate that prasugrel provides rapid and consistent inhibition of adenosine diphosphate-stimulated platelet aggregation and is well tolerated at the doses and time intervals studied.

SECTION: 15 Drug Metabolism and Body Distribution; 4 Toxicity; 6 Drug Evaluations
CLASSIFICATION: 20:12.04 Platelet aggregation inhibitors
INDEX TERM: CS-747; pharmacokinetics
INDEX TERM: Platelet aggregation; cs-747
INDEX TERM: Pharmacokinetics; cs-747
INDEX TERM: Bleeding time; cs-747
INDEX TERM: Blood levels; cs-747
INDEX TERM: Metabolism; cs-747
INDEX TERM: Toxicity; cs-747
INDEX TERM: Platelet aggregation inhibitors; cs-747
INDEX TERM: Drugs; new
INDEX TERM: Drug administration routes; oral
CAS REGISTRY NO.: **150322-43-3 (CS-747)**
CHEMICAL NAME: CS-747 (LY-640315); CS-747 (Prasugrel)

L53 ANSWER 14 OF 56 IPA COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:3127 IPA

DOCUMENT NUMBER: 39-03127
TITLE: CS-747 and R-99224
AUTHOR: Doggrell, S. A.; Mealy, N. E.; Castaner, J.
CORPORATE SOURCE: Reprints: Prous Sci., P.O. Box 540, 08080 Barcelona, Spain
SOURCE: Drugs of the Future (Spain), (Sep 2001) Vol. 26, pp. 835-840. 13 Refs.
CODEN: DRFUD4; ISSN: 0377-8282.
DOCUMENT TYPE: Journal
FILE SEGMENT: HUMAN
LANGUAGE: English
ABSTRACT:

An overview of CS-747 and its active metabolite R-99224, platelet aggregation inhibitors to prevent blood clotting in the coronary artery, is presented, including the synthesis, pharmacological actions, pharmacokinetics, metabolism, and clinical studies.

Elvira deC. Weiss
SECTION: 5 Investigational Drugs; 11 Pharmacology; 15 Drug Metabolism and Body Distribution
CLASSIFICATION: 20:12.04 Platelet aggregation inhibitors; 20:12.04 Platelet aggregation inhibitors
INDEX TERM: CS-747; overview
INDEX TERM: R-99224; metabolites; CS-747
INDEX TERM: Mechanism of action; CS-747; overview
INDEX TERM: Pharmacokinetics; CS-747; overview
INDEX TERM: Metabolism; CS-747; overview
INDEX TERM: Clinical studies; CS-747; overview
INDEX TERM: Platelet aggregation inhibitors; CS-747; overview
INDEX TERM: Platelet aggregation inhibitors; R-99224; overview
CAS REGISTRY NO.: **150322-43-3 (CS-747)**
CAS REGISTRY NO.: 239466-75-2 (R-99224)

L53 ANSWER 15 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:34344 BIOSIS
DOCUMENT NUMBER: PREV200600041967
TITLE: Stereoselective inhibition of human platelet aggregation by R-138727, the active metabolite of CS-747 (Prasugrel, LY640315), a novel P2Y(12) receptor inhibitor.
AUTHOR(S): Hasegawa, Michihiro; Sugidachi, Atsuhiro; Ogawa, Taketoshi; Isobe, Takashi; Jakubowski, Joseph A.; Asai, Fumitoshi [Reprint Author]
CORPORATE SOURCE: Sankyo Co Ltd, Pharmacol and Mol Biol Labs, Shinagawa Ku, 1-2-58 Hiromachi, Tokyo 1408710, Japan
toasai@sankyo.co.jp
SOURCE: Thrombosis and Haemostasis, (SEP 2005) Vol. 94, No. 3, pp. 593-598.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2005
Last Updated on STN: 28 Dec 2005

ABSTRACT:CS-747 (Prasugrel, LY640315) is a thienopyridine antiplatelet prodrug that is metabolized to the thiol-containing active metabolite R-138727, which binds to and irreversibly inhibits the platelet P2Y(12) ADP receptor. R-138727 is composed of 4 stereo-isomers, (R, S)-, (R, R)-, (S, S)-, and (S, R)-isomers (the first letter for the configuration of a chiral center at the sulfur-bearing position and the second for that at the benzylic position). In the present study, we determined the stereoselectivity of P2Y(12) antagonist effects by assessing the antagonism of the [H-3]-2-MeS-ADP that binds to human P2Y(12) receptors expressed in Chinese hamster ovary cells as an affinity

assay, and by the inhibition of ADP-induced aggregation of washed human platelets as a functional assay. R-138727 and its 2 components, R-99224,a mixture of (R, S)- and (S, R)-isomers and R-100364, a mixture of (R, R)and (S, S)-isomers, inhibited [3H]-2-MeS-ADP binding and platelet aggregation. The rank order of potency of these compounds were identical in both assays: R-99224 > R-138727 >> R-100364. Inhibition of ADP-induced platelet aggregation by R-138727 and R-99224 was concentration- and time-related. In experiments using the 4 single stereo-isomers, all isomers inhibited ADP-induced platelet aggregation, but the (R, S)-isomer was found to be the most potent, followed by the (R, R)-isomer. These in vitro studies indicate that R-138727 is an effective antagonist of P2Y(12), and potent inhibitor of ADP-induced platelet aggregation, and that these antiplatelet activities of R-138727 are largely dependent on its (R, S)-isomer. This suggests that the (R)configuration of the reactive thiol group of the active metabolite of CS-747 is critical for P2Y(12) and platelet inhibitory activities.

CONCEPT CODE: Cytology - Animal 02506
Cytology - Human 02508
Clinical biochemistry - General methods and applications 10006
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008

INDEX TERMS: Major Concepts
Pharmacology; Clinical Chemistry (Allied Medical Sciences); Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics

INDEX TERMS: Chemicals & Biochemicals
ADP; thiol; sulfur; P2Y12 receptor; platelet P2Y-12-ADP receptor; (R,S)-isomer; (R,R)-isomer; [tritiated]-2-MeS-ADP; CS-747 [LY640315, Prasugrel]: hematologic-drug; R-138727: hematologic-drug

INDEX TERMS: Miscellaneous Descriptors
stereoselective inhibition

ORGANISM: Classifier
Cricetidae 86310
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
CHO cell line (cell_line): Chinese hamster ovary cells
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 175832-20-9 (ADP)

Searched by Barb O'Bryen, STIC 2-2518

7704-34-9 (sulfur)
150322-43-3 (CS-747)
150322-43-3 (LY640315)
150322-43-3 (Prasugrel)

L53 ANSWER 16 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:191105 BIOSIS
DOCUMENT NUMBER: PREV200500192971
TITLE: Identification of the cytochromes P450 responsible for the formation of R-138727, the active metabolite of a novel thienopyridine anti-platelet agent, CS-747 (LY640315).
AUTHOR(S): Fayer, Jessica L. [Reprint Author]; Eckstein, James A.; Kasper, Steve C.; Farid, Nagy A.; Wrighton, Steven A.; Kurihara, Atsushi; Ring, Barbara J.
CORPORATE SOURCE: Lilly Res LabsDiv Drug Disposit, Eli Lilly and Co, Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism Reviews, (August 2004) Vol. 36, No. Suppl. 1, pp. 342. print.
Meeting Info.: 7th International Meeting of the International Society for the Study of Xenobiotics. Vancouver, BC, Canada. August 29-September 02, 2004. International Society for the Study of Xenobiotics.
ISSN: 0360-2532 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Digestive system - Physiology and biochemistry 14004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
Pharmacology - Cardiovascular system 22010
Immunology - General and methods 34502
INDEX TERMS: Major Concepts
Digestive System (Ingestion and Assimilation); Enzymology (Biochemistry and Molecular Biophysics); Pharmacology
INDEX TERMS: Parts, Structures, & Systems of Organisms
liver microsome: digestive system
INDEX TERMS: Chemicals & Biochemicals
CS-747 [LY640315]: antithrombotic-drug, cardiovascular-drug, hematologic-drug, novel theinopyridine anti-platelet agent, biotransformation; CYP2C19; CYP2C9; CYP3A; GSH; NADPH; R-138727; R-95913; cDNA [complementary DNA]; cytochrome P450 [EC 1.14.14.1]; dithiothreitol; monoclonal antibodies; reduced glutathione; sodium phosphate buffer
INDEX TERMS: Methods & Equipment

Searched by Barb O'Bryen, STIC 2-2518

Michaelis-Menten kinetics: mathematical and computer techniques
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
REGISTRY NUMBER: **150322-43-3** (CS-747)
150322-43-3 (LY640315)
70-18-8 (GSH)
53-57-6 (NADPH)
9035-51-2 (cytochrome P450)
9038-14-6 (cytochrome P450)
9035-51-2 (EC 1.14.14.1)
9038-14-6 (EC 1.14.14.1)
3483-12-3 (dithiothreitol)
70-18-8 (reduced glutathione)

L53 ANSWER 17 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:190908 BIOSIS
DOCUMENT NUMBER: PREV200500192774
TITLE: The disposition of CS-747 (LY640315), a novel thienopyridine, in mice.
AUTHOR(S): Gillespie, Todd A. [Reprint Author]; Smith, Richard L.; Rash, T. James; Ikeda, Toshihiko; Farid, Nagy A.
CORPORATE SOURCE: Div Drug Disposit, Lilly Res Labs, Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism Reviews, (August 2004) Vol. 36, No. Suppl. 1, pp. 242. print.
Meeting Info.: 7th International Meeting of the International Society for the Study of Xenobiotics. Vancouver, BC, Canada. August 29-September 02, 2004. International Society for the Study of Xenobiotics.
ISSN: 0360-2532 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Metabolism - General metabolism and metabolic pathways 13002
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Drug metabolism and metabolic stimulators 22003
INDEX TERMS: Major Concepts
Metabolism; Pharmaceuticals (Pharmacology)
INDEX TERMS: Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics
INDEX TERMS: Chemicals & Biochemicals
CS-747 [LY640315]: metabolic-drug, oral administration,

pharmacokinetics, thienopyridine, disposition, pharmaceutical

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: **150322-43-3** (CS-747)
150322-43-3 (LY640315)

L53 ANSWER 18 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:2929 BIOSIS
DOCUMENT NUMBER: PREV200400005090
TITLE: ADP receptors-targets for developing antithrombotic agents.
AUTHOR(S): Kunapuli, Satya P. [Reprint Author]; Ding, Zhongren; Dorsam, Robert T.; Kim, Soochong; Murugappan, Swaminathan; Quinton, Todd M.
CORPORATE SOURCE: Department of Physiology, Temple University Medical School, 3420 North Broad Street, Rm. 224OMS, Philadelphia, PA, 19140, USA
spk@temple.edu
SOURCE: Current Pharmaceutical Design, (2003) Vol. 9, No. 28, pp. 2303-2316. print.
ISSN: 1381-6128 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Dec 2003
Last Updated on STN: 17 Dec 2003
CONCEPT CODE: Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biophysics - Membrane phenomena 10508
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Blood and hematopoietic agents 22008
INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Cardiovascular System (Transport and Circulation); Pharmacology
INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics
INDEX TERMS: Chemicals & Biochemicals
ADP; CS-747: P2Y12 antagonist; P2X1; P2Y1; P2Y12; calcium channel; clopidogrel: hematologic-drug; platelet P2 receptor; ticlopidine: anticoagulant-drug, hematologic-drug
INDEX TERMS: Methods & Equipment
antithrombic treatment: clinical techniques, therapeutic and prophylactic techniques
INDEX TERMS: Miscellaneous Descriptors
platelet aggregation

Searched by Barb O'Bryen, STIC 2-2518

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common): animal model
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
REGISTRY NUMBER: 58-64-0Q (ADP)
4792-83-0Q (ADP)
7722-76-1Q (ADP)
19429-39-1Q (ADP)
175832-20-9Q (ADP)
150322-43-3 (CS-747)
113665-84-2 (clopidogrel)
55142-85-3 (ticlopidine)

L53 ANSWER 19 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:313326 BIOSIS
DOCUMENT NUMBER: PREV200200313326
TITLE: Platelet inhibitory effects of R-138727 the active metabolite of CS-747 a potent thienopyridyl P2Y12 antagonist prodrug.
AUTHOR(S): Jakubowski, Joseph A. [Reprint author]; Ogawa, Taketoshi; Sugidachi, Atsuhiro; Yoneda, Kenji; Iwamura, Ryo; Inoue, Teruhiko; Kimura, Tomio; Asai, Fumitoshi
CORPORATE SOURCE: BioMolecular Pharmacology, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A203. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 May 2002
Last Updated on STN: 29 May 2002
ABSTRACT:CS-747 is a thienopyridyl prodrug that is metabolized in vivo to an active platelet-inhibitory metabolite. We have identified R-138727 as an active metabolite of CS-747 and a potent antagonist of the P2Y12 platelet ADP receptor. In vitro studies were performed to evaluate the platelet inhibitory effects of R-138727. In human platelets, R-138727 inhibited ADP- and 2-MeS-ADP-induced platelet aggregation in a concentration- and time-dependent manner. R-138727 also inhibited collagen- and arachidonic acid-induced platelet aggregation but demonstrated minimal inhibition of thrombin peptide-induced aggregation. R-138727 consists of four optical isomers, and the previously described platelet-inhibitory metabolite R-99224 is a component of R-138727. While all the isomers of R-138727 inhibited ADP-induced platelet aggregation, the R,S enantiomer R-125690 was the most potent. The antiaggregatory potency of R-138727 was very similar to that of R-99224. These results show that R-138727 is an active metabolite of CS-747 and is a potent inhibitor of platelet aggregation. These observations are consistent with the effective antithrombotic activities that CS-747 provides following oral dosing.
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512

Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
Tissue culture, apparatus, methods and media 32500

INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelets: blood and lymphatics, drug treatment, in-vitro culture

INDEX TERMS: Chemicals & Biochemicals
R 138727: hematologic-drug, CS 747 metabolite, platelet aggregation inhibitor; thienopyridyl prodrug [CS 747]: hematologic-drug, platelet P-2Y-12 ADP receptor antagonist, platelet aggregation inhibitor

INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: normal blood donors
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: **150322-43-3** (CS 747)

L53 ANSWER 20 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:576047 BIOSIS
DOCUMENT NUMBER: PREV200100576047
TITLE: CS-747 and R-99224. Platelet antiaggregatory, P2T antagonist.
AUTHOR(S): Doggrell, S. A. [Reprint author]; Mealy, N. E.; Castaner, J.
CORPORATE SOURCE: Department of Physiology and Pharmacology, The University of Queensland, Brisbane, Qld, 4072, Australia
SOURCE: Drugs of the Future, (September, 2001) Vol. 26, No. 9, pp. 835-840. print.
ISSN: 0377-8282.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2001
Last Updated on STN: 25 Feb 2002
CONCEPT CODE: Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Pathology - Therapy 12512
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Cardiovascular system 22010

INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelets: blood and lymphatics, shape change

Searched by Barb O'Bryen, STIC 2-2518

INDEX TERMS: Diseases
vascular injury: injury, vascular disease
INDEX TERMS: Chemicals & Biochemicals
ADP: platelet agonist; CS-747: cardiovascular-drug, P2T antagonist, platelet antiaggregatory, synthesis; R-99224: cardiovascular-drug, P2T antagonist, platelet antiaggregatory, synthesis; granule contents: secretion
INDEX TERMS: Miscellaneous Descriptors
bloodstream
REGISTRY NUMBER: 58-64-0Q (ADP)
4792-83-0Q (ADP)
7722-76-1Q (ADP)
19429-39-1Q (ADP)
175832-20-9Q (ADP)
150322-43-3 (CS-747)
204204-74-0 (R-99224)

L53 ANSWER 21 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:160957 BIOSIS
DOCUMENT NUMBER: PREV200100160957
TITLE: Antiplatelet action of R-99224, an active metabolite of a novel thienopyridine-type Gi-linked P2T antagonist, CS-747.
AUTHOR(S): Sugidachi, Atsuhiro; Asai, Fumitoshi [Reprint author]; Yoneda, Kenji; Iwamura, Ryo; Ogawa, Taketoshi; Otsuguro, Ken-ichi; Koike, Hiroyuki
CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo, 140-8710, Japan
toasai@shina.sankyo.cp.jp
SOURCE: British Journal of Pharmacology, (Janaury, 2001) Vol. 132, No. 1, pp. 47-54. print.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2001
Last Updated on STN: 15 Feb 2002

ABSTRACT:1 CS-747 is a novel thienopyridine-type platelet ADP inhibitor which lacks in vitro activity. This study examined pharmacological profiles of R-99224, a hepatic metabolite of CS-747. 2 R-99224 produced a concentration-dependent inhibition of in vitro platelet aggregation in washed human platelets (0.03-1 mug ml-1), which was relatively specific to ADP compared to collagen and thrombin. 3 R-99224 (0.1 - 3 mug ml-1) also elicited a similar inhibition of ADP-induced aggregation in rat platelets. The inhibition by R-99224 (10 mug ml-1) persisted even after platelets were washed three times. Intravenous injection of R-99224 (0.1 - 3 mg kg-1) to rats resulted in a dose-dependent inhibition of ex vivo ADP-induced platelet aggregation. 4 R-99224 (0.1 - 100 muM) decreased binding of (3H)-2-methylthio-ADP((3H)-2-MeS-ADP), a stable ligand for platelet ADP receptors, to washed human platelets. The inhibition by R-99224 reached a plateau at a concentration of 3 muM (1.4 mug ml-1), but complete inhibition was not achieved even at the highest concentration used (100 muM). 5 R-99224 (10 muM) in combination with ARL-66096 (0.3 muM), an ATP analogue-type Gi-linked P2T receptor antagonist, produced no additional inhibition of (3H)-2-MeS-ADP binding. In contrast, (3H)-2-MeS-ADP binding was completely abolished by R-99224 (10 muM) in combination with A3P5PS (300 muM), a selective P2Y1 antagonist, suggesting that R-99224 selectively binds to the Gi-linked P2T receptor. 6 R-99224 (0.01 - 3 mug ml-1) inhibited ADP-induced (125I)-fibrinogen binding to human platelets in a concentration-dependent manner. R-99224 (0.1 - 1 mug ml-1) also inhibited the ADP-induced decrease in cyclic AMP levels in PGE1-stimulated platelets, whereas

the agent did not affect ADP (10 muM)-induced Ca2+ mobilization. 7 These findings suggest that R-99224 is a selective and irreversible antagonist of Gi-linked P2T receptors and that R-99224 is a responsible molecule for in vivo actions of CS-747.

CONCEPT CODE: Pharmacology - Blood and hematopoietic agents 22008
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005

INDEX TERMS: Major Concepts
Pharmacology; Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics, aggregation, inhibition

INDEX TERMS: Chemicals & Biochemicals
CS-747: anticoagulant-drug, thienopyridine-type
G-i-linked P2T antagonist; G-i-linked P2T receptors;
R-99224: Cs-747 metabolite, antiplatelet action

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat: male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: **150322-43-3** (CS-747)
204204-74-0 (R-99224)

L53 ANSWER 22 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:235332 BIOSIS
DOCUMENT NUMBER: PREV200000235332
TITLE: The in vivo pharmacological profile of CS-747, a novel antiplatelet agent with platelet ADP receptor antagonist properties.
AUTHOR(S): Sugidachi, Atsuhiro; Asai, Fumitoshi [Reprint author]; Ogawa, Taketoshi; Inoue, Teruhiko; Koike, Hiroyuki
CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Sankyo Co., Ltd, 1-2-58 Hiromachi, Shinagawa-ku, Tokyo, 140-8710, Japan
SOURCE: British Journal of Pharmacology, (April, 2000) Vol. 129, No. 7, pp. 1439-1446. print.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002

ABSTRACT:1 CS-747 is a novel antiplatelet agent that generates an active

metabolite, R-99224, in vivo. CS-747 itself was totally inactive in vitro. This study examined in vitro pharmacological profiles of CS-747 after single oral administration to rats. 2 Orally administered CS-747 (0.3-10 mg kg-1) partially but significantly decreased (3H)-2-methylthio-ADP binding to rat platelets. CS-747 (3 mg kg-1, p.o.) treatment neutralized ADP-induced decreases of cyclic AMP concentrations induced by prostaglandin E1, suggesting that metabolites of CS-747 interfere with Gi-linked P2T receptor. 3 CS-747 (0.3 and 3 mg kg-1, p.o.) markedly inhibited ex vivo washed platelet aggregation in response to ADP but not to thrombin. CS-747 also exhibited a marked inhibition of ADP-induced ex vivo platelet aggregation in PRP with a rapid onset (<0.5 h) and long duration (>3 days) of action (ED50 at 4 h=1.2 mg kg-1). 4 R-99224 (IC50=45 muM) inhibited in vitro PRP aggregation in a concentration-related manner. 5 CS-747 prevented thrombus formation in a dose-related manner with an ED50 value of 0.68 mg kg-1. CS-747 was more potent than clopidogrel (6.2 mg kg-1) and ticlopidine (>300 mg kg-1). 6 CS-747, clopidogrel, and ticlopidine prolonged the bleeding time. The order of potency of these agents in this activity was the same as that in antiaggregatory and antithrombotic activities. 7 These findings indicate that CS-747 is an orally active and a potent antiplatelet and antithrombotic agent with a rapid onset and long duration of action, and warrants clinical evaluations of the agent.

CONCEPT CODE: Pharmacology - General 22002
Cytology - Animal 02506
Biochemistry studies - General 10060
Metabolism - General metabolism and metabolic pathways 13002
Cardiovascular system - General and methods 14501
Blood - General and methods 15001

INDEX TERMS: Major Concepts
Pharmacology; Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics

INDEX TERMS: Chemicals & Biochemicals
ADP; CS-747: anticoagulant-drug, hematologic-drug, antiplatelet agent, pharmacological profile; R-99224: metabolite; clopidogrel; cyclic AMP; prostaglandin E-1; thrombin; ticlopidine

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat: male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 58-64-0Q (ADP)
4792-83-0Q (ADP)
7722-76-1Q (ADP)
19429-39-1Q (ADP)
175832-20-9Q (ADP)
150322-43-3 (CS-747)
204204-74-0 (R-99224)
113665-84-2 (clopidogrel)
60-92-4 (cyclic AMP)
745-65-3 (prostaglandin E-1)
9002-04-4 (thrombin)
55142-85-3 (ticlopidine)

L53 ANSWER 23 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on

STN
ACCESSION NUMBER: 1999:191247 BIOSIS
DOCUMENT NUMBER: PREV199900191247
TITLE: Efficacy of CS-747, a new potent antiplatelet agent.
AUTHOR(S): Hirota, T. [Reprint author]; Sugii, H.; Asai, F.; Kawabata, K.; Inoue, T.; Iwamura, R.; Freestone, S.; Dickson, J.
CORPORATE SOURCE: Sankyo Co. Ltd., Ube Industries Ltd., Tokyo, Japan
SOURCE: Clinical Pharmacology and Therapeutics, (Feb., 1999) Vol. 65, No. 2, pp. 148. print.
Meeting Info.: One-hundredth Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics. San Antonia, Texas, USA. March 18-20, 1999. American Society for Clinical Pharmacology and Therapeutics.
CODEN: CLPTAT. ISSN: 0009-9236.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999
CONCEPT CODE: Pharmacology - General 22002
Metabolism - General metabolism and metabolic pathways 13002
Cardiovascular system - General and methods 14501
General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
INDEX TERMS: Major Concepts
Cardiovascular System (Transport and Circulation); Pharmacology
INDEX TERMS: Diseases
angina: heart disease
Angina Pectoris (MeSH)
INDEX TERMS: Diseases
myocardial infarction: heart disease, vascular disease
Myocardial Infarction (MeSH)
INDEX TERMS: Diseases
stroke: nervous system disease, vascular disease
Cerebrovascular Disorders (MeSH)
INDEX TERMS: Chemicals & Biochemicals
CS-747: antiplatelet agent, efficacy
INDEX TERMS: Miscellaneous Descriptors
pharmacokinetics; Meeting Abstract
REGISTRY NUMBER: **150322-43-3** (CS-747)

L53 ANSWER 24 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:124751 TOXCENTER
COPYRIGHT: Copyright 2006 ACS
DOCUMENT NUMBER: CA14413226296E
TITLE: Oral prophylactic agents for thrombosis and embolism
AUTHOR(S): Morishima, Yoshiyuki; Watanabe, Kengo
CORPORATE SOURCE: ASSIGNEE: Daiichi Seiyaku Co., Ltd.
PATENT INFORMATION: JP 200652208 A2 23 Feb 2006
SOURCE: (2006) Jpn. Kokai Tokkyo Koho, 29 pp.
CODEN: JKXXAF.
COUNTRY: JAPAN
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2006:170095
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 14 Mar 2006

Searched by Barb O'Bryen, STIC 2-2518

Last Updated on STN: 9 May 2006

ABSTRACT:
Title agents contain diamines I [Q1 = (un)substituted 4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl, 4,5,6,7-tetrahydrothiazolo[4,5-c]pyridin-2-yl, 4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl, 4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl, 4,6-dihydro-5H-pyrrolo[3,4-d]thiazol-2-yl, etc.; Q2 = C1-8 alkylene, (CH2)pA(CH2)q (p, q = 1-3; p + q = 2-4); A = O, N, S, SO, SO2, NH; R1, R2 = H, OH, NH2, CO2H, (halo)alkyl, acyl, alkoxycarbonylalkyl, (un)substituted acylamino, (un)substituted 3- to 6-membered heterocyclylcarbonyl, etc.; Q3 = CO, SO2, COCONH, CSCONH, COCSNH, CSCSNH; Q4 = (un)substituted Ph, naphthyl, pyridyl, pyrimidyl, indolyl, benzothienyl, furyl, etc.] and antiplatelet agents chosen from aspirin, sarpogrelate, limaprost, cilostazol, and piperidines II or III [R101, R105 = H, lower alkyl, lower alkoxycarbonyl, lower alkylcarbonyl; R102, R103, R106, R107 = H, lower alkyl, halo; R104 = H, OH, lower alkylcarbonyloxy; R108 = H, lower alkyl; R109 = H, lower alkylcarbonyl] as active ingredients. Thus, combination use of N1-(5-chloropyridin-2-yl)-N2-[(1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-[[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino]cyclohexyl]ethanediamide HCl salt (IV) and ticlopidine prevented 75% thrombosis formation in rats. CYP2D6- and CYP3A4-dependent metabolism of IV was 0.1-0.81 pmol/pmol/CYP/min, suggesting nonsusceptibility of IV to the enzymes.
CLASSIFICATION CODE: 1-8
SUPPLEMENTARY TERMS: Miscellaneous Descriptors
oral prophylaxis antithrombotic antiplatelet combination; ticlopidine cyclohexylethanediamide combination antithrombotic oral prophylaxis
REGISTRY NUMBER: 50-78-2 (Aspirin)
50-78-2Q (Aspirin, mixts. contg.)
55142-85-3 (Ticlopidine)
55142-85-3Q (Ticlopidine, mixts. contg.)
73963-72-1 (Cilostazol)
73963-72-1Q (Cilostazol, mixts. contg.)
74397-12-9 (Limaprost)
74397-12-9Q (Limaprost, mixts. contg.)
113665-84-2 (Clopidogrel)
113665-84-2Q (Clopidogrel, mixts. contg.)
125926-17-2 (Sarpogrelate)
125926-17-2Q (Sarpogrelate, mixts. contg.)
150322-43-3Q (mixts. contg.)
REGISTRY NUMBER: 480448-29-1; **150322-43-3**

L53 ANSWER 25 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:260164 TOXCENTER
COPYRIGHT: Copyright (c) 2006 The Thomson Corporation
DOCUMENT NUMBER: 42-17755
TITLE: Randomized comparison of Prasugrel (CS- 747, LY640315), a novel thienopyridine P2Y<INF>12</INF> antagonist, with clopidogrel in percutaneous coronary intervention - Results of the joint utilization of medications to block platelets optimally (JUMBO)-TIMI 26 trial
AUTHOR(S): Wiviott, SD; Antman, EM; Winters, KJ; Weerakkody, G; JUMBO-TIMI 26 Investigators; et al
CORPORATE SOURCE: Harvard Univ, Div Cardiovasc, 75 Francis St, Boston, MA 02115, USA swiviott@partners.org
SOURCE: Circulation, (2005) Vol. 111, pp. 3366-3373. 31 Refs. CODEN: CIRCAZ. ISSN: 0009-7322.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 2005:17729

LANGUAGE: English
ENTRY DATE: Entered STN: 4 Oct 2005
Last Updated on STN: 4 Oct 2005
ABSTRACT:
To compare the antiplatelet efficacy and safety of prasugrel (CS-747, LY-640315) with clopidogrel in percutaneous coronary intervention, a phase II clinical study was performed. Patients (n=904) were randomized to either standard dosing with or 1 of 3 prasugrel regimens. Subjects were monitored for 30 days for bleeding and clinical events. Hemorrhagic complications were infrequent, with no significant difference between patients treated with prasugrel or clopidogrel in the rate of significant bleeding.
SECTION CODE: 5 Investigational Drugs; 4 Toxicity
CLASSIFICATION CODE: 20:12.04 Platelet aggregation inhibitors; 20:12.04 Platelet aggregation inhibitors
SUPPLEMENTARY TERMS: Miscellaneous Descriptors
CS-747; coronary disease
Clopidogrel; coronary disease
Platelet aggregation inhibitors; cs-747
Platelet aggregation inhibitors; clopidogrel
Drug comparisons; cs-747 and clopidogrel
Drug comparisons; clopidogrel and cs-747
Dosage; cs-747
Toxicity; cs-747
Coronary disease; cs-747
Dosage; clopidogrel
Toxicity; clopidogrel
Coronary disease; clopidogrel
Drugs; new
Interventions; coronary disease
REGISTRY NUMBER: **150322-43-3** (CS-747)
113665-84-2 (Clopidogrel)
CHEMICAL NAME: CS-747 (Prasugrel); CS-747 (LY-640315)

L53 ANSWER 26 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:10603 TOXCENTER
COPYRIGHT: Copyright 2006 ACS
DOCUMENT NUMBER: CA13607096057Z
TITLE: Tetrahydrothienopyridine derivative acid addition salts
AUTHOR(S): Asai, Fumitoshi; Ogawa, Taketoshi; Naganuma, Hideo; Yamamura, Naotoshi; Inoue, Teruhiko; Nakamura, Kazuyoshi
CORPORATE SOURCE: ASSIGNEE: Ube Industries, Ltd.
PATENT INFORMATION: WO 2002004461 A1 17 Jan 2002
SOURCE: (2002) PCT Int. Appl., 33 pp.
CODEN: PIXXD2.
COUNTRY: JAPAN
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2002:51473
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 22 Jan 2002
Last Updated on STN: 9 Dec 2003
ABSTRACT:
Claimed are acid addition salts of 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine. These acid addition salts exhibit excellent peroral absorbability, metabolism-activating and platelet aggregation-inhibiting effects, low toxicity, and excellent storage and handling stabilities, and are useful as drugs for thrombosis and infarction. Oral administration of 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine maleic acid salt at 0.3 mg/kg to dogs gave 58.6±15.7% inhibition of platelet aggregation at 4 h after said

administration, vs. 23.8±12.6% platelet aggregation inhibition caused by 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (free base) at 0.3 mg/kg orally. Formulations are given.
CLASSIFICATION CODE: 1-8
SUPPLEMENTARY TERMS: Miscellaneous Descriptors
tetrahydrothienopyridine deriv acid salt thrombosis infarction remedy
REGISTRY NUMBER: 108-24-7 (Acetic anhydride)
110-16-7 (Maleic acid)
446-48-0 (2-Fluorobenzyl bromide)
5500-21-0 (Cyclopropyl cyanide)
7439-95-4 (Magnesium)
7647-01-0 (Hydrochloric acid)
67-64-1 (Acetone)
REGISTRY NUMBER: **389574-19-0**; **389574-20-3**; **150322-43-3**; 115473-15-9; 150322-38-6; 150322-73-9; 204205-33-4

L53 ANSWER 27 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:143127 TOXCENTER
COPYRIGHT: Copyright 2006 ACS
DOCUMENT NUMBER: CA13314187474N
TITLE: CS-747, a new platelet ADP receptor antagonist
AUTHOR(S): Asai, Fumitoshi; Konse, Tomonori; Sugidachi, Atsuhiro; Ikeda, Toshihiko; Sanbuissho, Atsushi; Hirota, Takashi
CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Product Development Laboratories, SANKYO CO., LTD., Tokyo, 140-8710, Japan.
SOURCE: Annual Report of Sankyo Research Laboratories, (1999) Vol. 51, pp. 1-44.
CODEN: ASRLEC. ISSN: 1341-741X.
COUNTRY: JAPAN
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2000:288118
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 26 Mar 2002
ABSTRACT:
A review with 29 refs. on physicochem. properties and pharmacol. of the title antiplatelet agent.
CLASSIFICATION CODE: 1-0
SUPPLEMENTARY TERMS: Miscellaneous Descriptors
review platelet ADP receptor antagonist CS747 antiplatelet
REGISTRY NUMBER: **150322-43-3** (CS 747)

L53 ANSWER 28 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:104474 TOXCENTER
COPYRIGHT: Copyright 2006 ACS
DOCUMENT NUMBER: CA12808093213W
TITLE: Novel medicinal compositions of hydropyridines
AUTHOR(S): Asai, Fumitoshi; Ogawa, Taketoshi; Inoue, Teruhiko
CORPORATE SOURCE: ASSIGNEE: Ube Industries, Ltd.
PATENT INFORMATION: WO 9749397 A1 31 Dec 1997
SOURCE: (1997) PCT Int. Appl., 47 pp.
CODEN: PIXXD2.
COUNTRY: JAPAN
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS

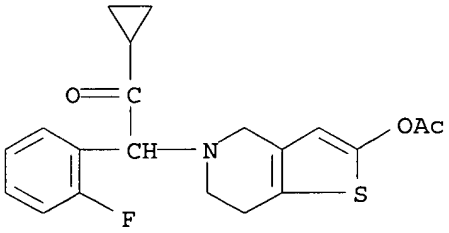
OTHER SOURCE: CAPLUS 1998:42276
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 9 Mar 2004

ABSTRACT:
The invention relates to compns. containing as the active ingredient 4,5,6,7-tetrahydrothieno[3,2-c]pyridines represented by the following general formula : R1-CH(R2)-R3 or pharmacol. acceptable salts thereof which have an excellent effect of inhibiting the progression of arteriosclerosis and a low toxicity and, therefore, are highly useful as remedies or preventives for arteriosclerosis. In said formula, R1 represents optionally substituted phenyl; R2 represents H, alkoxycarbonyl or optionally substituted aliphatic acyl; and R3 represents optionally substituted 4,5,6,7-tetrahydrothieno[3,2-c]pyridin-5-yl.

CLASSIFICATION CODE: 63-6
SUPPLEMENTARY TERMS: Miscellaneous Descriptors
antiarteriosclerotic hydropyridine pharmaceutical
REGISTRY NUMBER: 90055-48-4; 90055-76-8; 109904-27-0; 109904-29-2; 150322-13-7; 150322-15-9; 150322-19-3; 150322-38-6; 150322-40-0; 150322-42-2; **150322-43-3**; 150322-44-4; 150322-45-5; 150322-46-6; 150322-51-3; 150322-59-1; 150322-62-6; 150322-63-7; 150322-64-8; 150322-65-9; 178688-44-3; 201049-72-1; 201049-73-2; 201049-74-3; 201049-75-4; 201049-76-5; 201049-77-6; 201049-78-7

L53 ANSWER 29 OF 56 IMSRESEARCH COPYRIGHT 2006 IMSWORLD on STN

ACCESSION NUMBER: 1998:226 IMSRESEARCH
SOURCE: R&D Focus, (8 May 2006)
GENERIC NAME: prasugrel
REFERENCE: pINN
LABORATORY NAME: CS 747; LY 640315
CHEMICAL NAME: 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclop ropyl-2-(2-fluorophenyl)ethanone
CAS REGISTRY NO.: **150322-43-3**
STRUCTURE:



DERIVATIVE(S): **150322-43-3**prasugrel
CLASSIFICATION: B1C Platelet Aggregation Inhibitors; C1D Coronary Therapy
INDICATION: coronary artery disease; thrombosis; cardiovascular disease; stroke; ischemia; myocardial infarction; heart ischemia; angina
ACTION: platelet antiaggregant; purinoceptor antagonist
HIGHEST DEV. PHASE: Phase III (50)
LATEST INFORMATION: UPDATE: Analyst prediction. ....In a presentation at Lilly's Investment Community Update, 9 December 2004, New

York, USA, Steven Paul, Executive VP, Science & Technology at Lilly, announced that Lilly and Sankyo have initiated enrollment of a multicenter, worldwide, phase III trial, known as TRITON-TIMI 38, of prasugrel. The trial is expected to enroll over 13 000 patients with acute coronary syndrome (heart attacks and/or unstable angina) who are to undergo percutaneous coronary intervention (PCI). Lilly anticipates an NDA submission in the USA late 2006 for the treatment of acute coronary syndrome. Prasugrel, an oral antithrombotic prodrug, inhibits the ADP receptor.

CURRENT DEVELOPMENT STATUS:

Type	Status	Stage	Region	Indication
Highest Phase	Phase III	50		
Phase	Phase III		Worldwide	coronary artery disease
Phase	Phase II		United States	ischemia
Phase	Phase II		Europe	ischemia
Phase	Phase I		Japan	ischemia

COMPANY INFORMATION:

Type	Company	Nationality
Originator	Daiichi Sankyo	Japan
Co-developer	Ube	Japan
Other	Lilly	United States
Assignee	Sankyo : Ube	

ESTIMATED LAUNCH: 2007 United States
2007 Europe

PATENT SUMMARY:
Product: EP 542411 B 1998, priority JP 227875 1991, designating 17 states. Equivalents identified in 17 countries.

COMMERCIAL SUMMARY:
Prasugrel, an oral antithrombotic prodrug discovered by Daiichi Sankyo (formerly known as Sankyo) and Ube, inhibits the ADP receptor and is being developed for use in the treatment of acute coronary syndrome in patients who have suffered a heart attack or have angina. Lilly and Daiichi Sankyo have initiated an international phase III trial of prasugrel in conjunction with Harvard Medical School (USA) and Brigham and Women's Hospital (USA) (Lilly, DEC 2004). The trial, designated TRITON-TIMI 38, aims to enroll 13 000 patients with acute coronary syndrome (heart attacks and/or unstable angina), who are to undergo percutaneous coronary intervention (PCI). The aim of the trial is to evaluate the ability of prasugrel to prevent heart attack, stroke and death in patients who undergo PCI compared with clopidogrel. The secondary endpoints include impact on bleeding, recurrent ischemia and need for additional procedures to restore blood flow (Lilly, Sankyo, OCT 2004). Lilly has completed a multicenter, interventional phase II trial in the USA, which compared

prasugrel with clopidogrel in 904 patients aged 18-75 years undergoing percutaneous coronary intervention (PCI) (Lilly, FEB 2004) and results have been reported (Lilly, Sankyo, AUG 2004). Lilly anticipates filing a regulatory submission for marketing approval in the second half of 2007 (Lilly, DEC 2005). Lilly was planning to conduct phase III trials of the agent in acute coronary syndrome and stroke, and dependent on a successful outcome, expected a regulatory submission in the USA late 2006 (Lilly, DEC 2004). Phase II trials are under way in Europe and the USA under co-development with Lilly to evaluate the agent as a treatment for ischemic disease (Sankyo, JAN 2004). Phase II trials were planned to commence second quarter 2003 for acute coronary syndrome and cerebrovascular accident (Sankyo, FEB 2003). Phase I trials have been conducted in Japan, the USA (Sankyo, JUN 2002) and Europe (Sankyo, NOV 1999). The product is also to be developed for secondary prevention of thrombotic cardiovascular complications in patients with recent ischemic stroke or unstable angina and myocardial infarction, as well as for reducing secondary complications such as myocardial infarction, recurrent stroke and rehospitalization for severe angina. Sankyo (now known as Daiichi Sankyo) and Lilly have signed a letter of intent, under which Sankyo will receive a signing fee, milestone payments and royalties on product sales. Under the proposed agreement, prasugrel will be co-marketed by Lilly and Sankyo except in certain countries where Lilly will receive exclusive sales and marketing rights. The product will be co-promoted by both companies in the USA. Additionally, both companies plan to share in the development of the compound, whilst Ube will manufacture the bulk material (Lilly, DEC 2000). Daiichi Sankyo predicts launches for the product in the USA and Europe during 2007 with peak sales of around YEN100 billion (Sankyo, MAY 2002). (Ube review ed, AUG 1998; Sankyo confirmed phase I, Japan, ischemic disease, JAN 2004; Sankyo confirmed phase III ongoing, worldwide, acute coronary syndrome, MAY 2005) Latest prediction Analyst, Credit Suisse, reporting on Lilly, predicts the release of data from a phase III trial of prasugrel first half 2007; estimates sales of US$240.1 million in 2008, US$567.1 million in 2009 and US$992.7 million in 2010 (Credit Suisse, APR 2006). >Bear Stearns Analyst, Bear Stearns, reporting on Lilly, estimates worldwide sales for prasugrel of US$300 million in 2008, US$609 million in 2009 and US$1.041 billion in 2010 (Bear Stearns, SEP 2005). Credit Suisse First Boston Analyst, Credit Suisse First Boston, reporting on Daiichi Sankyo, estimates sales for CS 747 (prasugrel) of YEN950 billion in FYE March 2009 (Credit Suisse First Boston, DEC 2005). >Analyst, Credit Suisse First Boston, reporting on Lilly, estimates sales for prasugrel of US$214.6 million in 2007 and US$1.226 billion in 2010 (Credit Suisse First Boston, JUN 2005). >Analyst, Credit Suisse First Boston, reporting on Lilly, predicts a 2007 launch for prasugrel and estimates peak sales of US$1.5 billion (Credit Suisse First Boston, DEC 2004). JPMorgan Analyst, JPMorgan, reporting on Sankyo (now known as Daiichi Sankyo), predicts a regulatory filing for CS 747 (prasugrel) first half 2007 and estimates sales of YEN15 billion in FYE March 2009 and peak sales of over YEN100 billion (JPMorgan, NOV 2004). Merrill Lynch Analyst, Merrill Lynch, predicts a launch in 2006 (Merrill Lynch, JUN 2002). Morgan Stanley Analyst, Morgan Stanley, reporting on Daiichi Sankyo, estimates total sales for CS 747 (prasugrel) of YEN10.7 billion in FY2008 and YEN21 billion in FY2009 (Morgan Stanley, SEP 2005). >Analyst, Morgan Stanley, reporting on Sankyo (now known as Daiichi Sankyo) predicts a regulatory filing for CS 747 (prasugrel) in 2006 (Morgan Stanley, MAR 2005). Analyst, Morgan Stanley, reporting on Lilly, estimates sales for prasugrel of US$100 million in 2008 (Morgan Stanley, APR 2004). >Analyst, Morgan Stanley, reporting on Lilly, estimates sales for prasugrel of US$100 million in 2008 and US$350 million in 2009 (Morgan Stanley, OCT 2005).

SCIENTIFIC SUMMARY:
Preclinical studies showed that prasugrel was metabolized to its active component efficiently (Lilly, FEB 2004). In clinical studies, prasugrel demonstrated a high level of platelet inhibition (Lilly, FEB 2004). Results

from a phase II trial comparing prasugrel to clopidogrel, involving 904 patients who had suffered a heart attack or heart-related chest pain, showed a non-significant reduction in major adverse cardiovascular events (death, heart attack and stroke), in patients treated with prasugrel for 30 days, compared to patients treated with clopidogrel. There were no significant differences in bleeding for the prasugrel and clopidogrel arms of the trial. Prasugrel demonstrated a comparable safety profile to clopidogrel (Eli Lilly, Sankyo, AUG 2004). Three phase I trials showed that prasugrel prevented platelet aggregation better than clopidogrel, with less variability in terms of response rates and inhibition of platelet aggregation in prasugrel-treated patients. In a trial in 68 healthy subjects, a greater than 25% inhibition of platelet aggregation was achieved in all patients treated with a 60 mg loading dose of prasugrel compared with 42.4% of patients administered the approved 300 mg loading dose of clopidogrel. In a trial in 30 male volunteers administered once-daily maintenance doses of prasugrel (5, 10, or 20 mg), clopidogrel (75 mg), or placebo, the maximum level of platelet inhibition after ten days was greater for all prasugrel doses than with clopidogrel or placebo. In a trial in 101 aspirin-treated patients with stable atherosclerotic vascular disease, significantly higher levels of platelet inhibition were achieved in patients receiving 40 and 60 mg prasugrel loading doses compared with those on a 300 mg clopidogrel loading dose. After 28 days, higher levels of platelet inhibition were recorded in patients on prasugrel 10 and 15 mg maintenance doses compared with those on 75 mg clopidogrel. There was a trend towards more bruising and minor bleeding with the 15 mg prasugrel maintenance dose (Lilly, MAR 2005). Pooled results from three early-phase single-center trials in a total of 112 healthy volunteers (aged 18-65 years) randomized to loading doses of either 60 mg prasugrel or 300 mg clopidogrel in a two-way cross-over design showed that while all subjects responded to prasugrel not all of the same subjects responded to clopidogrel, according to objectively defined parameters for inhibition of platelet aggregation (IPA). ADP was used to induce platelet aggregation in samples of subjects' blood, and IPA and change in maximum platelet aggregation (MPA) from baseline were evaluated at 4-5 h and 24 h after drug administration. Nonresponders were defined as those achieving less than 25% IPA or a difference of less than 20% in MPA in response to 5 mcm ADP, and less than 20% IPA or a difference of less than 15% in MPA to 20 mcm ADP. While all subjects responded to prasugrel, 22% and 43% were nonresponders to clopidogrel according to IPA with 5 mcm and 20 mcm ADP respectively (Lilly, OCT 2005). In a phase Ib trial in which 81 aspirin-treated patients with stable cardiovascular disease were randomized to either the 300 mg approved loading dose of clopidogrel or 40 mg or 60 mg prasugrel, inhibition of platelet aggregation and change in maximum platelet aggregation from baseline were evaluated 6 h after drug administration. More than 90% of prasugrel patients compared with less than 50% of clopidogrel patients achieved greater than 20% inhibition of platelet aggregation. Even patients with more reactive platelets at baseline (which may be less affected or unaffected by thienopyridine therapies) had higher and more consistent inhibition of platelet aggregation following prasugrel. In a second study in which blood from nine healthy donors, pre- and post-aspirin therapy, was incubated with varying concentrations of active prasugrel metabolites (with ADP used to induce platelet activation and aggregation), rapid, potent and consistent inhibition of both platelet activation and generation of thrombo-inflammatory markers was achieved, independent of the effects of aspirin. Pre-treatment with aspirin did not appear to be required for prasugrel blockade of ADP-induced platelet activation (Lilly, MAR 2006).

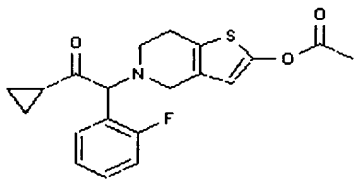
DEVELOPMENT HISTORY:

OCT 2005	Daiichi merged with Sankyo to form Daiichi Sankyo.
NOV 2004	Phase III, Worldwide (coronary artery disease).
JAN 2004	Phase II, USA, Europe (ischemia).
2003	Phase II, USA (coronary artery disease).

JUN 2002 Phase I, USA, Japan.
DEC 2000 Letter of intent signed between Sankyo and Lilly.
FEB 1998 Phase I, Europe.
SEP 1991 Priority product patent application filed in Japan, by Sankyo and Ube.

L53 ANSWER 30 OF 56 PROUSDDR COPYRIGHT 2006 PROUS SCIENCE on STN
ACCESSION NUMBER: 1999:3152 PROUSDDR
DOCUMENT NUMBER: 273686
CHEMICAL NAME: Acetic acid 5-(2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridin-2-yl ester
DRUG NAME: CS-747
LY-640315
GENERIC NAME: Prasugrel (Prop INN, USAN)
CAS REGISTRY NUMBER: **150322-43-3**
389574-19-0 (hydrochloride)
MOLECULAR FORMULA: C20 H20 F N O3 S
STATUS: Actively Investigated
HIGHEST DEV. PHASE: PHASE III
ORIGINATOR: Sankyo
Ube
LICENSEE: Lilly
CLASSIFICATION CODE: Antiplatelet Therapy
ACTION MECHANISM: P2Y12 (P2T) Antagonists
OTHER SOURCE: SYNTHLINE 2001001093; PROUSDDR 2001004790 (Metabolite); 343867 (Metabolite); 343880 (Metabolite); 349314 (Metabolite); 349316 (Metabolite)
ENTRY DATE: Entered STN: 9 May 2004
Last Updated on STN: 4 Aug 2006

STRUCTURE:



PROUS REFERENCES:
RefID: 527623 (Text Available)
Drug Data Report, Vol. 21, No. 4, pp 323, 1999

RefID: 636139
Drugs of the Future, Vol. 26, No. 9, pp 835, 2001

REFERENCE TEXT: RefID: 527623
ACTION - Antiplatelet agent, a potent P2T purinoceptor antagonist. Phase I clinical trials in healthy volunteers demonstrated that a single oral dose of compound (30 or 75 mg) produced rapid (1 h) and long-lasting inhibition (> 48 h) of ex vivo ADP- but not collagen-induced platelet aggregation. In a multiple-dose study, 10 mg p.o. inhibited platelet aggregation for at least 2 days after treatment. Compound was devoid of serious side effects.

Searched by Barb O'Bryen, STIC 2-2518

Potentially useful for the treatment or prevention of cardiovascular events such as unstable angina, myocardial infarction or stroke.

PATENT REFERENCES:

TITLE: Novel medicinal compositions of hydropyridines
INVENTOR(S): Ogawa, T.; Inoue, T.; Asai, F.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: JP 98310586 19981124
WO 9749397 19971231
PRIORITY INFORMATION: JP 1996-166126 19960626
JP 1997-54587 19970310

TITLE: 2-Silyloxytetrahydrothienopyridine, salt thereof and process for preparing the same
INVENTOR(S): Yamamoto, Y.; Miyata, H.; Ataka, K.; Kohno, M.; Yokota, N.
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: US 5874581 19990223
WO 9611203 19960418
PRIORITY INFORMATION: JP 1994-244141 19941007

TITLE: Hydropyridine derivative acid addition salts
INVENTOR(S): Nakamura, K.; Ogawa, T.; Inoue, T.; Asai, F.; Naganuma, H.; Yamamura, N.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: EP 1298132 20030402
JP 2002145883 20020522
US 2003134872 20030717
US 6693115 20040217
WO 2002004461 20020117
PRIORITY INFORMATION: JP 2000-205396 20000706
JP 2000-266780 20000904

TITLE: Medicinal compositions containing aspirin
INVENTOR(S): Ogawa, T.; Inoue, T.; Asai, F.; Sugidachi, A.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: JP 2002255814 20020911
WO 2002051412 20020704
PRIORITY INFORMATION: JP 2000-392983 20001225

TITLE: Medicines containing acid additive salts of hydropyridine derivatives
INVENTOR(S): Nakamura, K.; Ogawa, T.; Inoue, T.; Asai, F.; Naganuma, H.; Yamamura, N.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: JP 2003246735 20030902
PRIORITY INFORMATION: JP 2001-388757 20011221

TITLE: Medicinal composition for treating arteriosclerosis
INVENTOR(S): Ogawa, T.; Inaba, T.; Asai, F.
PATENT ASSIGNEE(S): Sankyo
PATENT INFORMATION: JP 2004051639 20040219
WO 2004009119 20040129
PRIORITY INFORMATION: JP 2002-209165 20020718

TITLE: Treating cardiovascular diseases with a compound of formula 1 (CS 747 - prasugrel; RN 150322-43-4)
INVENTOR(S): Jakubowski, J.A.; Farid, N.A.; Brandt, J.T.; Winters, K.J.
PATENT ASSIGNEE(S): Lilly
PATENT INFORMATION: EP 1660183 20060531
WO 2004098713 20041118
PRIORITY INFORMATION: US 2003-467903 20030505

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Hirota, T.; Sugii, H.; Asai, F.; Kawabata, K.; Inoue, T.; Iwamura, R.; Freestone, S.; Dickson, J., Annu Meet Am Soc Clin Pharmacol Ther (ASCPT) (100th Edition), March 18 1999-March 20 1999, San Antonio, (Abst PII-5)

(2) RefID: 547186, Periodic Publication
"Antithrombotic and antiplatelet effects of CS-747, a novel P2T antagonist"
Asai, F.; Sugidachi, A.; Ogawa, T.; Nagasawa, T.; Shimoji, T.; Suzuki, N.; Kawamura, Y.; Inoue, T.; Iwamura, R., Thromb Haemost, No. Suppl., (Abst 2626), 1999

(3) RefID: 547188, Periodic Publication
"Pharmacokinetics and disposition of CS-747, a new pro-drug ADP-receptor antagonist, in rats and dogs"
Ikeda, T.; Iwabuchi, H.; Kawabata, K.; Tsutsumi, S.; Suzuki, N.; Sone, J.; Yoneda, K.; Kita, J., Thromb Haemost, No. Suppl., (Abst 2627), 1999

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Sugidachi, A.; Asai, F.; Ogawa, T.; Inoue, T.; Koike, H., Br J Pharmacol, Vol. 129, No. 7, pp 1439, 2000

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Sugidachi, A.; Asai, F.; Yoneda, K.; Iwamura, R.; Ogawa, T.; Otsuguro, K.; Koike, H., Br J Pharmacol, Vol. 132, No. 1, pp 47, 2001

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"Antiplatelet, antithrombotic and antihemostatic effects of multiple administration of CS-747, a novel P2TAC receptor antagonist, in rats"
Otsuguro, K.; Asai, F.; Sugidachi, A.; Ogawa, T.; Nagasawa, T.; Shimoji, T.; Suzuki, N.; Fujisawa, Y.; Nakanishi, Y.; Inoue, T., Thromb Haemost, No. Suppl., (Abst P1901), 2001

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"The P2TAC receptor antagonistic actions of CS-747 and its metabolite, R-99224, in rats"
Asai, F.; Ogawa, T.; Sugidachi, A.; Otsuguro, K.; Shimoji, T.; Suzuki, N.; Fuisawa, Y.; Yoneda, K.; Iwamura, R., Thromb Haemost, No. Suppl., (Abst P1915), 2001

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Searched by Barb O'Bryen, STIC 2-2518

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Ding, Z.; Kim, S.; Dorsam, R.T.; Jin, T.; Kunapuli, S.P., Blood, Vol. 101, No. 10, pp 3908, 2003

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Asai, F.; Niitsu, Y.; Ogawa, T.; et al., J Thromb Haemost, Vol. 1, No. Suppl. 1, (Abst P2033), 2003

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"Anti-platelet and anti-thrombotic effects of CS-747, a novel P2Y12 receptor antagonist, in combination with aspirin"
Sugidachi, A.; Ogawa, T.; Isobe, T.; Shimoji, T.; Suzuki, N.; Kakusaka, M.; Asai, F., J Thromb Haemost, Vol. 1, No. Suppl. 1, (Abst P2032), 2003

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"Superior responder rate for inhibition of platelet aggregation with a 60 mg loading dose of prasugrel (CS-747, LY640315) compared with a 300 mg loading dose of clopidogrel"
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(25) RefID: 917736, Congress Literature
"Superior inhibition of platelet aggregation following a loading Dose of CS-747 (Prasugrel, LY640315) versus clopidogrel: Correlation with the pharmacokinetics of active metabolite generation"
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"Effect of ketoconazole on the pharmacokinetics and pharmacodynamics of CS-747 (LY640315, Prasugrel) and clopidogrel in healthy subjects"
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"Potent inhibition of platelet aggregation by prasugrel (CS-747, LY640315), a novel thienopyridine antiplatelet agent, is associated with covalent binding of active metabolite to ADP receptor"
Kurihara, A.; et al., ESC Congress, Sept 3 2005-Sept 7 2005, Stockholm, (Abst P2960)

(30) RefID: 923892, Congress Literature
"Prasugrel (CS-747), a novel thienopyridine P2Y12 receptor antagonist, results in more effective platelet inhibition than clopidogrel in aspirin-treated patients with atherosclerotic disease"
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(31) RefID: 923893, Congress Literature
"Pharmacokinetics and pharmacodynamics of prasugrel (CS-747, LY640315), a novel thienopyridine P2Y12 receptor antagonist, in healthy subjects"
Payne, C.D.; et al., ESC Congress, Sept 3 2005-Sept 7 2005, Stockholm, (Abst P3512)

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"Platelet inhibition and pharmacokinetics following prasugrel (CS-747, LY640315), a novel thienopyridine P2Y12 receptor antagonist, or clopidogrel in healthy, aspirin-treated subjects"
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Weerakkody, G.J.; Brandt, J.T.; Payne, C.D.; Jakubowski, J.A.; Farid, N.A.; Naganuma, H.; Winters, K.J., Am J Cardiol, Vol. 96, No. 7, Suppl. 1, (Abst TCT-32), 2005

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Brandt, J.T.; Payne, C.D.; Weerakkody, G.J.; Small, D.S.; Naganuma, H.; Jakubowski, J.A.; Farid, N.A.; Wiviott, S.D.; Winters, K.J., Am J Cardiol, Vol. 96, No. 7, Suppl. 1, (Abst TCT-376), 2005

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"Prasugrel (CS-747) achieves significantly higher inhibition of platelet aggregation and a lower rate of non-responders compared with clopidogrel in aspirin-treated patients with atherosclerotic vascular disease"
Winters, K.J.; Jernberg, T.; Leese, P.T.; Nilsson, L.-G.; Payne, C.D.; Darstein, C.; Brandt, J.T.; Jakubowski, J.A.; Siegbahn, A.; Wallentin, L., Am J Cardiol, Vol. 96, No. 7, Suppl. 1, (Abst TCT-388), 2005

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"The active metabolite of prasugrel (CS-747) inhibits ADP-stimulated thrombo-inflammatory markers of platelet activation: Leukocyte-platelet and platelet-platelet aggregation and platelet surface P-selectin and activated GPIIb-IIIa"
Frelinger, A.L. III.; Jakubowski, J.A.; Li, Y.F.; Barnard, M.R.; Fox, M.L.; Linden, M.D.; Sugidachi, A.; Winters, K.J.; Furman, M.I.; Michelson, A.D., Circulation, Vol. 112, No. 17, Suppl. 2, (Abst 1904), 2005

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Morrow, D.A.; Sabatine, M.S.; Wiviott, S.D.; Murphy, S.A.; Winters, K.J.; Antman, E.M.; Braunwald, E., Circulation, Vol. 112, No. 17, Suppl. 2, (Abst 2094), 2005

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"Stereoselective inhibition of human platelet aggregation by R-138727, the active metabolite of CS-747 (prasugrel, LY640315), a novel P2Y12 receptor inhibitor"
Hasegawa, M.; Sugidachi, A.; Ogawa, T.; Isobe, T.; Jakubowski, J.A.; Asai, F., Thromb Haemost, Vol. 94, No. 3, pp 593, 2005

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"The active metabolite of Prasugrel (CS-747) inhibits adenosine diphosphate-stimulated thromboinflammatory markers of platelet activation: modulation by other blood cells and calcium, but not by aspirin"
Frelinger, A.L.; et al., J Am Coll Cardiol, Vol. 47, No. 4, Suppl. 1, (Abst 1023-161), 2006

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"The influence of baseline platelet aggregation response on subsequent inhibition of aggregation achieved with clopidogrel or prasugrel"
Jakubowski, J.A.; Weerakkody, G.J.; Winters, K.J.; Brandt, J.T.; Naganuma, H.; Wallentin, L., J Am Coll Cardiol, Vol. 47, No. 4, Suppl. 1, (Abst 855-3), 2006

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"Increasing concentrations of prasugrel's active metabolite produce

increased inhibition of platelet aggregation"
Small, D.S.; Payne, C.D.; Ferguson-Sells, L.R.; Farid, N.A.; Naganuma, H.; Darstein, C.; Wallentin, L.; Winters, K.J., J Am Coll Cardiol, Vol. 47, No. 4, Suppl. 1, (Abst 855-6), 2006

(45) RefID: 987763, Periodic Publication
"The platelet inhibitory effects and pharmacokinetics of prasugrel after administration of loading and maintenance doses in healthy subjects"
Jakubowski, J.A.; Payne, C.D.; Brandt, J.T.; Weerakkody, G.J.; Farid, N.A.; Small, D.S.; Naganuma, H.; Li, G.Y.; Winters, K.J., J Cardiovasc Pharmacol, Vol. 47, No. 3, pp 377, 2006

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"Prasugrel achieves greater inhibition of platelet aggregation and a lower rate of non-responders compared with clopidogrel in aspirin-treated patients with stable coronary artery disease"
Jernberg, T.; Payne, C.D.; Winters, K.J.; Darstein, C.; Brandt, J.T.; Jakubowski, J.A.; Naganuma, H.; Siegbahn, A.; Wallentin, L., Eur Heart J, Vol. 27, No. 10, pp 1166, 2006

(47) RefID: 1006478, Periodic Publication
"Platelet inhibitory activity and pharmacokinetics of prasugrel (CS-747) a novel thienopyridine P2Y12 inhibitor: A single ascending dose study in healthy humansdagger"
Asai, F.; Jakubowski, J.A.; Naganuma, H.; Brandt, J.T.; Matsushima, N.; Hirota, T.; Freestone, S.; Winters, K.J., Platelets, Vol. 17, No. 4, pp 209, 2006

(48) RefID: 1006479, Periodic Publication
"Platelet inhibitory activity and pharmacokinetics of prasugrel (CS-747) a novel thienopyridine P2Y12 inhibitor: A multiple-dose study in healthy humansdagger"
Matsushima, N.; Jakubowski, J.A.; Asai, F.; Naganuma, H.; Brandt, J.T.; Hirota, T.; Freestone, S.; Winters, K.J., Platelets, Vol. 17, No. 4, pp 218, 2006

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ACCESSION NUMBER:	2006194112 EMBASE
TITLE:	The Year in Interventional Cardiology.
AUTHOR:	Dixon S.R.; Grines C.L.; O'Neill W.W.
CORPORATE SOURCE:	Dr. W.W. O'Neill, William Beaumont Hospital, Royal Oak, MI, United States. woneill@beaumont.edu
SOURCE:	Journal of the American College of Cardiology, (18 Apr 2006) Vol. 47, No. 8, pp. 1689-1706. . Refs: 132 ISSN: 0735-1097 CODEN: JACCDI
PUBLISHER IDENT.:	S 0735-1097(06)00445-1
COUNTRY:	United States
DOCUMENT TYPE:	Journal; General Review
FILE SEGMENT:	018 Cardiovascular Diseases and Cardiovascular Surgery 027 Biophysics, Bioengineering and Medical Instrumentation 037 Drug Literature Index 038 Adverse Reactions Titles

039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 May 2006
Last Updated on STN: 23 May 2006
ABSTRACT: The Year in Interventional Cardiology. Simon R. Dixon, Cindy L. Grines, William W. O'Neill. .COPYRGT. 2006 American College of Cardiology Foundation.

CONTROLLED TERM: Medical Descriptors:
*interventional cardiovascular procedure
acute heart infarction: DT, drug therapy
acute heart infarction: SU, surgery
acute heart infarction: TH, therapy
percutaneous coronary intervention
blood clot lysis
heart muscle revascularization
heart failure
coronary stent
angioplasty
ST segment elevation
bleeding: SI, side effect
drug safety
low drug dose
intermethod comparison
stroke
drug megadose
thrombectomy
heart catheterization
stem cell transplantation
nuclear magnetic resonance imaging
heart ejection fraction
cardiogenic shock: CO, complication
acute coronary syndrome
coronary artery disease: SU, surgery
coronary artery disease: TH, therapy
coronary artery bypass graft
drug eluting stent
treatment outcome
heart muscle ischemia: TH, therapy
restenosis: CO, complication
restenosis: DM, disease management
restenosis: DT, drug therapy
restenosis: PC, prevention
restenosis: RT, radiotherapy
saphenous vein graft
thrombosis: CO, complication
cost effectiveness analysis
brachytherapy
artery intima proliferation: CO, complication
biocompatibility
balloon occlusion
aorta disease: TH, therapy
carotid artery disease: TH, therapy
drug hypersensitivity: SI, side effect
thrombocyte aggregation
drug eruption: SI, side effect
human
clinical trial
review

priority journal

CONTROLLED TERM: Drug Descriptors:
tissue plasminogen activator: AE, adverse drug reaction
tissue plasminogen activator: CT, clinical trial
tissue plasminogen activator: DO, drug dose
tissue plasminogen activator: DT, drug therapy
reteplase: CT, clinical trial
reteplase: DT, drug therapy
tenecteplase: AE, adverse drug reaction
tenecteplase: CT, clinical trial
tenecteplase: DO, drug dose
tenecteplase: DT, drug therapy
clopidogrel: AE, adverse drug reaction
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
heparin: CT, clinical trial
heparin: CM, drug comparison
heparin: DO, drug dose
heparin: DT, drug therapy
abciximab: AE, adverse drug reaction
abciximab: CT, clinical trial
abciximab: CB, drug combination
abciximab: DT, drug therapy
adenosine: CT, clinical trial
adenosine: DO, drug dose
adenosine: DT, drug therapy
adenosine: IV, intravenous drug administration
nicorandil: CT, clinical trial
nicorandil: DT, drug therapy
nicorandil: IV, intravenous drug administration
nicorandil: PD, pharmacology
granulocyte colony stimulating factor: CT, clinical trial
granulocyte colony stimulating factor: CB, drug combination
granulocyte colony stimulating factor: DT, drug therapy
granulocyte colony stimulating factor: IV, intravenous drug administration
granulocyte colony stimulating factor: PD, pharmacology
vasculotropin: AE, adverse drug reaction
vasculotropin: CT, clinical trial
vasculotropin: DT, drug therapy
vasculotropin: IM, intramuscular drug administration
vasculotropin: PD, pharmacology
plasmid DNA: AE, adverse drug reaction
plasmid DNA: CT, clinical trial
plasmid DNA: DT, drug therapy
plasmid DNA: IM, intramuscular drug administration
plasmid DNA: PD, pharmacology
monoclonal antibody cd 34: CT, clinical trial
monoclonal antibody cd 34: DT, drug therapy
monoclonal antibody: CT, clinical trial
monoclonal antibody: DT, drug therapy
rapamycin: CT, clinical trial
rapamycin: CM, drug comparison
rapamycin: DT, drug therapy
rapamycin: PR, pharmaceutics
paclitaxel: CT, clinical trial
paclitaxel: CM, drug comparison
paclitaxel: DT, drug therapy

paclitaxel: PR, pharmaceutics
abt 578: CT, clinical trial
abt 578: DT, drug therapy
abt 578: PR, pharmaceutics
everolimus: CT, clinical trial
everolimus: DT, drug therapy
everolimus: PR, pharmaceutics
cilostazol: AE, adverse drug reaction
cilostazol: CT, clinical trial
cilostazol: CB, drug combination
cilostazol: DT, drug therapy
cilostazol: PO, oral drug administration
cilostazol: PD, pharmacology
pioglitazone: CT, clinical trial
pioglitazone: DT, drug therapy
pioglitazone: PO, oral drug administration
pioglitazone: PD, pharmacology
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
ticlopidine: AE, adverse drug reaction
ticlopidine: CT, clinical trial
ticlopidine: CB, drug combination
ticlopidine: DT, drug therapy
prasugrel: AE, adverse drug reaction
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
enoxaparin: CT, clinical trial
enoxaparin: CB, drug combination
enoxaparin: DT, drug therapy
fondaparinux: AE, adverse drug reaction
fondaparinux: CT, clinical trial
fondaparinux: DT, drug therapy
unclassified drug

CAS REGISTRY NO.: (tissue plasminogen activator) 105913-11-9; (reteplase) 133652-38-7; (tenecteplase) 191588-94-0; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (abciximab) 143653-53-6; (adenosine) 58-61-7; (nicorandil) 65141-46-0; (vasculotropin) 127464-60-2; (rapamycin) 53123-88-9; (paclitaxel) 33069-62-4; (everolimus) 159351-69-6; (cilostazol) 73963-72-1; (pioglitazone) 105355-27-9, 111025-46-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) **389574-19-0**; (enoxaparin) 9041-08-1; (fondaparinux) 104993-28-4, 114870-03-0

NAME OF PRODUCT: (1) Cypher; (2) 'Taxus'; aspirin

COMPANY NAME: Otsuka (United States); Takeda (Japan)

COMPANY NAME: (1) Johnson and Johnson; (2) Boston Scientific; Medtronic (Italy) ; Sorin (United States) ; Kensey Nash (United States) ; St Jude

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ACCESSION NUMBER: 2006163293 EMBASE

TITLE: Clopidogrel treatment prior to **percutaneous coronary** intervention: When enough isn't enough.

AUTHOR: Steinhubl S.R.; Charnigo R.
CORPORATE SOURCE: Dr. S.R. Steinhubl, 326 Charles T. Wethington Bldg, 900 S Limestone St, Lexington, KY 40536-0200, United States. steinhubl@uky.edu
SOURCE: Journal of the American Medical Association, (5 Apr 2006) Vol. 295, No. 13, pp. 1581-1582. .
Refs: 20
ISSN: 0098-7484 E-ISSN: 1538-3598 CODEN: JAMAAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2006
Last Updated on STN: 25 Apr 2006
CONTROLLED TERM: Medical Descriptors:
***percutaneous coronary intervention**
acute coronary syndrome: DT, drug therapy
acute coronary syndrome: SU, surgery
acute coronary syndrome: TH, therapy
unstable angina pectoris: DT, drug therapy
unstable angina pectoris: SU, surgery
unstable angina pectoris: TH, therapy
heart infarction: DT, drug therapy
heart infarction: SU, surgery
heart infarction: TH, therapy
Q wave
transluminal coronary angioplasty
drug activity
drug effect
risk reduction
thrombocyte aggregation inhibition
drug efficacy
treatment duration
revascularization
coronary stent
ST segment elevation
human
clinical trial
editorial
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: CT, clinical trial
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
heparin: CT, clinical trial
heparin: CM, drug comparison
heparin: DT, drug therapy
heparin: PD, pharmacology
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
abciximab: CT, clinical trial
abciximab: DT, drug therapy
abciximab: PD, pharmacology

eptifibatide: CT, clinical trial
eptifibatide: DT, drug therapy
eptifibatide: PD, pharmacology
tirofiban: CT, clinical trial
tirofiban: DT, drug therapy
ticlopidine: CT, clinical trial
ticlopidine: DT, drug therapy
troponin T: EC, endogenous compound
low molecular weight heparin: DT, drug therapy
antithrombocytic agent: DT, drug therapy
prasugrel: DT, drug therapy
cangrelor: DT, drug therapy
cangrelor: PA, parenteral drug administration
thrombin inhibitor: DT, drug therapy
azd 6140
sch 530348

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (abciximab) 143653-53-6; (eptifibatide) 148031-34-9; (tirofiban) 142373-60-2, 144494-65-5, 150915-40-5; (ticlopidine) 53885-35-1, 55142-85-3; (troponin T) 60304-72-5; (prasugrel) **389574-19-0**

CHEMICAL NAME: Azd 6140; Sch 530348

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ACCESSION NUMBER: 2006163286 EMBASE

TITLE: Abciximab in patients with acute **coronary** syndromes undergoing **percutaneous** **coronary** intervention after clopidogrel pretreatment: The ISAR-REACT 2 randomized trial.

AUTHOR: Kastrati A.; Mehilli J.; Neumann F.-J.; Dotzer F.; Ten Berg J.; Bollwein H.; Graf I.; Ibrahim M.; Pache J.; Seyfarth M.; Schuhlen H.; Dirschinger J.; Berger P.B.; Schomig A.

CORPORATE SOURCE: Dr. A. Kastrati, Deutsches Herzzentrum, Lazarettstrasse 36, 80636 Munich, Germany. kastrati@dhm.mhn.de

SOURCE: Journal of the American Medical Association, (5 Apr 2006) Vol. 295, No. 13, pp. 1531-1538. .
Refs: 41
ISSN: 0098-7484 E-ISSN: 1538-3598 CODEN: JAMAAP

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 25 Apr 2006
Last Updated on STN: 25 Apr 2006

ABSTRACT: Context: No specifically designed studies have addressed the role of the glycoprotein IIb/IIIa inhibitor abciximab in patients with non-ST-segment elevation acute **coronary** syndromes (ACS) undergoing ***percutaneous*** **coronary** intervention (**PCI**) after pretreatment with 600 mg of clopidogrel. Objective: To assess whether abciximab is associated with clinical benefit in highrisk patients with ACS undergoing **PCI** after pretreatment with 600 mg of clopidogrel. Design, Setting, and Patients: International, multicenter, randomized,

doubleblind, placebo-controlled study conducted from March 2003 through December 2005, enrolling 2022 patients (mean age, 66 years) with non-ST-segment elevation ACS undergoing **PCI**. Interventions: Patients were assigned to receive either abciximab (0.25 mg/kg of body weight bolus, followed by a 0.125-μg/kg per minute [maximum, 10 μg/min] infusion for 12 hours, plus heparin, 70 U/kg of body weight) or placebo (placebo bolus and infusion of 12 hours, plus heparin bolus, 140 U/kg). All patients received clopidogrel, 600 mg, at least 2 hours prior to the procedure, as well as 500 mg of oral or intravenous aspirin. Main Outcome Measures: The primary end point was a composite of death, myocardial infarction, or urgent target vessel revascularization occurring within 30 days after randomization; secondary end points were rates of in-hospital major and minor bleeding. Results: Of 2022 patients enrolled, 1012 were assigned to abciximab and 1010 to placebo. The primary end point was reached in 90 patients (8.9%) assigned to abciximab vs 120 patients (11.9%) assigned to placebo, a 25% reduction in risk with abciximab (relative risk [RR], 0.75; 95% CI, 0.58-0.97; P=.03). Among patients without an elevated troponin level, there was no difference in the incidence of primary end point events between the abciximab group (23/499 patients [4.6%]) and the placebo group (22/474 patients [4.6%]) (RR, 0.99; 95% CI, 0.56-1.76; P=.98), whereas among patients with an elevated troponin level, the incidence of events was significantly lower in the abciximab group (67/513 patients [13.1%]) compared with the placebo group (98/536 patients [18.3%]), which corresponds to an RR of 0.71 (95% CI, 0.54-0.95; P=.02) (P=.07 for interaction). There were no significant differences between the 2 groups regarding the risk of major and minor bleeding as well as need for transfusion. Conclusions: Abciximab reduces the risk of adverse events in patients with non-ST-segment elevation ACS undergoing **PCI** after pretreatment with 600 mg of clopidogrel. The benefits provided by abciximab appear to be confined to patients presenting with an elevated troponin level.

CONTROLLED TERM: Medical Descriptors:
***acute coronary syndrome: DT, drug therapy**
***acute coronary syndrome: TH, therapy**
percutaneous coronary intervention
ST segment elevation
drug effect
high risk patient
bolus injection
outcome assessment
treatment outcome
heart death: SI, side effect
heart infarction: SI, side effect
revascularization: SI, side effect
bleeding: SI, side effect
hospitalization
risk reduction
incidence
drug efficacy
drug binding
electrocardiogram
drug safety
demography
thrombocytopenia: SI, side effect
human
male
female
major clinical study
clinical trial
randomized controlled trial

Searched by Barb O'Bryen, STIC 2-2518

double blind procedure
multicenter study
controlled study
aged
adult
article
priority journal

CONTROLLED TERM: Drug Descriptors:
*abciximab: AE, adverse drug reaction
*abciximab: CT, clinical trial
*abciximab: AD, drug administration
*abciximab: CB, drug combination
*abciximab: DO, drug dose
*abciximab: DT, drug therapy
*abciximab: PD, pharmacology
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: DO, drug dose
heparin: DT, drug therapy
placebo
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: IV, intravenous drug administration
acetylsalicylic acid: PO, oral drug administration
troponin: EC, endogenous compound
beta adrenergic receptor blocking agent: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
nitrate: DT, drug therapy
calcium antagonist: DT, drug therapy
prasugrel
cangrelor
azd 6140

CAS REGISTRY NO.: (abciximab) 143653-53-6; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (nitrate) 14797-55-8; (prasugrel) **389574-19-0**

CHEMICAL NAME: Azd 6140

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ACCESSION NUMBER: 2006345426 EMBASE
TITLE: Clopidogrel resistance: Implications for coronary stenting.
AUTHOR: Gurbel P.A.; Lau W.C.; Bliden K.P.; Tantry U.S.
CORPORATE SOURCE: P.A. Gurbel, Sinai Center for Thrombosis Research, 2401 W. Belvedere Ave., Baltimore, MD 21215, United States. Pgurbel@lifebridgehealth.org
SOURCE: Current Pharmaceutical Design, (2006) Vol. 12, No. 10, pp. 1261-1269. .
Refs: 56
ISSN: 1381-6128 CODEN: CPDEFP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology

036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Aug 2006
Last Updated on STN: 10 Aug 2006

ABSTRACT: Clopidogrel, in combination wih aspirin, is currently the drug of choice to prevent thrombosis after coronary stent implantation. Currently, clopidogrel is administered to the vast majority of patients without any assessment of platelet inhibition. Response variability and resistance, however, definitely occur to clopidogrel treatment. Preliminary data support the hypothesis that patients with reactive or clopidogrel nonresponsive platelets are at risk for thrombotic events. However, the magnitude of the clinical effect remains unknown and relationship between nonresponsiveness and risk of clinical events is under-investigated. Several important questions that must be answered are: A) What is the relation of clopidogrel resistance and high platelet reactivity to the occurrence of stent thrombosis, recurrent myocardial infarction, stroke and death?; B) Is there a threshold of platelet reactivity that correlates with the onset of thrombotic risk?; and C) What is the cost of administering clopidogrel to non-responsive patients? Finally, our understanding of the clinical relevance of drug resistance and high platelet reactivity should be facilitated by the use of validated point-of-service devices. The mechanisms of the response variability to clopidogrel remain incompletely defined. The contribution of intra- and extracellular pathways are under investigation. .COPYRGT. 2006 Bentham Science Publishers Ltd.

CONTROLLED TERM: Medical Descriptors:

***coronary stent**
***coronary artery thrombosis: CO, complication**
***coronary artery thrombosis: DM, disease management**
***coronary artery thrombosis: DR, drug resistance**
***coronary artery thrombosis: DT, drug therapy**
***coronary artery thrombosis: PC, prevention**
drug choice
drug efficacy
cardiovascular risk
thrombocyte function
heart infarction
recurrent disease
cerebrovascular accident
mortality
drug cost
dose response
thrombocyte activation
anticoagulation
drug mechanism
drug metabolism
calcium cell level
thrombocyte aggregation inhibition
drug antagonism
drug potentiation
cardiotoxicity: SI, side effect
acute coronary syndrome: DT, drug therapy
high risk patient
drug dose regimen
maintenance drug dose
breath analysis
drug megadose
protein function

protein phosphorylation
human
nonhuman
clinical trial
review
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: AE, adverse drug reaction
*clopidogrel: CT, clinical trial
*clopidogrel: CB, drug combination
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PE, pharmacoeconomics
*clopidogrel: PK, pharmacokinetics
*clopidogrel: PD, pharmacology
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
adenosine diphosphate: EC, endogenous compound
thrombocyte receptor: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
purine P2Y1 receptor: EC, endogenous compound
fibrinogen receptor: EC, endogenous compound
calcium: EC, endogenous compound
prasugrel
atorvastatin: AE, adverse drug reaction
atorvastatin: CT, clinical trial
atorvastatin: CB, drug combination
atorvastatin: CM, drug comparison
atorvastatin: IT, drug interaction
atorvastatin: DT, drug therapy
atorvastatin: PK, pharmacokinetics
cytochrome P450 3A4: EC, endogenous compound
pravastatin: CB, drug combination
pravastatin: IT, drug interaction
pravastatin: PK, pharmacokinetics
erythromycin: CT, clinical trial
erythromycin: CB, drug combination
erythromycin: CM, drug comparison
erythromycin: DO, drug dose
erythromycin: IT, drug interaction
rifampicin: CT, clinical trial
rifampicin: CB, drug combination
rifampicin: CM, drug comparison
rifampicin: DO, drug dose
rifampicin: IT, drug interaction
antibiotic agent: CT, clinical trial
antibiotic agent: CB, drug combination
antibiotic agent: CM, drug comparison
antibiotic agent: DO, drug dose
antibiotic agent: IT, drug interaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: AE, adverse drug reaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: CT, clinical trial
hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
hydroxymethylglutaryl coenzyme A reductase inhibitor: CM,

drug comparison
hydroxymethylglutaryl coenzyme A reductase inhibitor: IT, drug interaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy
hydroxymethylglutaryl coenzyme A reductase inhibitor: PK, pharmacokinetics
heparin
fibrinogen receptor antagonist
troleandomycin: IT, drug interaction
troleandomycin: DT, drug therapy
troleandomycin: TO, drug toxicity
abciximab: CT, clinical trial
abciximab: IT, drug interaction

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (adenosine diphosphate) 20398-34-9, 58-64-0; (calcium) 7440-70-2; (prasugrel) **389574-19-0**; (atorvastatin) 134523-00-5, 134523-03-8; (cytochrome P450 3A4) 329736-03-0; (pravastatin) 81131-74-0; (erythromycin) 114-07-8, 70536-18-4; (rifampicin) 13292-46-1; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (troleandomycin) 2751-09-9; (abciximab) 143653-53-6

CHEMICAL NAME: (1) Cs 747; Aspirin

COMPANY NAME: (1) Sankyo (Japan)

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ACCESSION NUMBER: 2006240444 EMBASE

TITLE: Prasugrel achieves greater inhibition of platelet aggregation and a lower rate of non-responders compared with clopidogrel in aspirin-treated patients with stable coronary artery disease.

AUTHOR: Jernberg T.; Payne C.D.; Winters K.J.; Darstein C.; Brandt J.T.; Jakubowski J.A.; Naganuma H.; Siegbahn A.; Wallentin L.

CORPORATE SOURCE: L. Wallentin, Department of Medical Sciences, Cardiology and Uppsala Clinical Research Center, University Hospital, 751 85 Uppsala, Sweden. lars.wallentin@ucr.uu.se

SOURCE: European Heart Journal, (2006) Vol. 27, No. 10, pp. 1166-1173. .
Refs: 22
ISSN: 0195-668X E-ISSN: 1522-9645 CODEN: EHJODF

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 19 Jun 2006
Last Updated on STN: 19 Jun 2006

ABSTRACT: Aims: This study was designed to compare the degree of inhibition of platelet aggregation (IPA) of prasugrel with that of clopidogrel in stable aspirin-treated patients with coronary artery disease (CAD). Methods and results Subjects (n = 101) were randomly assigned to the following loading dose (LD) (day 1)/ maintenance dose (MD) (days 2-28) combinations: prasugrel, 40

mg/5 mg; 40 mg/7.5 mg; 60 mg/10 mg; 60 mg/15 mg; or clopidogrel, 300 mg/75 mg. Turbidometric platelet aggregation was measured at multiple timepoints during the study. At 4 h after dosing, with 20 μM ADP, both prasugrel LDs achieved significantly higher mean IPA levels (60.6% and 68.4 vs. 30.0%, respectively; all P < 0.0001) and lower percentage (3 vs. 52%, P < 0.0001) of pharmacodynamic non-responders (defined as IPA <20%) than clopidogrel. Prasugrel 10 and 15 mg MDs achieved consistently higher mean IPA than clopidogrel 75 mg at day 28 (all P < 0.0001). At pre-MD on day 28, there were no non-responders in the 10 and 15 mg prasugrel group, compared with 45% in the clopidogrel group (P = 0.0007). Conclusion: In this population, prasugrel (40-60 mg LD and 10-15 mg MD) achieves greater IPA and a lower proportion of pharmacodynamic non-responders compared with the approved clopidogrel dosing.

CONTROLLED TERM: Medical Descriptors:
*thrombocyte aggregation inhibition
***coronary artery disease: DT, drug therapy**
maintenance drug dose
turbidimetry
skin bruising: SI, side effect
bleeding: SI, side effect
epistaxis: SI, side effect
gingiva bleeding: SI, side effect
hemoptysis: SI, side effect
blister: SI, side effect
wound: SI, side effect
conjunctival hemorrhage: SI, side effect
hematuria: SI, side effect
human
male
female
clinical trial
randomized controlled trial
single blind procedure
multicenter study
controlled study
aged
adult
article
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: AE, adverse drug reaction
*clopidogrel: CT, clinical trial
*clopidogrel: CB, drug combination
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
***acetylsalicylic acid: CT, clinical trial**
***acetylsalicylic acid: CB, drug combination**
***acetylsalicylic acid: DT, drug therapy**
*prasugrel: AE, adverse drug reaction
*prasugrel: CT, clinical trial
*prasugrel: CB, drug combination
*prasugrel: CM, drug comparison
*prasugrel: DO, drug dose
*prasugrel: DT, drug therapy

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (prasugrel) **389574-19-0**

CHEMICAL NAME: (1) Ecotrin; (2) Plavix; Cs 747
COMPANY NAME: (1) Glaxo SmithKline; (2) Sanofi Synthelabo; Sankyo (Japan)

L53 ANSWER 36 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006211534 EMBASE
TITLE: P2Y(12) receptor antagonists: A rapidly expanding group of antiplatelet agents.
AUTHOR: Cattaneo M.
CORPORATE SOURCE: M. Cattaneo, Unita di Ematologia e Trombosi, Ospedale San Paolo-Universita di Milano, Via di Rudini 8, 20142 Milano, Italy. marco.cattaneo@unimi.it
SOURCE: European Heart Journal, (2006) Vol. 27, No. 9, pp. 1010-1012. .
Refs: 10
ISSN: 0195-668X E-ISSN: 1522-9645 CODEN: EHJODF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 31 May 2006
Last Updated on STN: 31 May 2006
CONTROLLED TERM: Medical Descriptors:
pharmacodynamics
drug safety
thrombocyte aggregation inhibition
ischemic heart disease: DT, drug therapy
bleeding: SI, side effect
dyspnea: SI, side effect
human
clinical trial
editorial
priority journal
CONTROLLED TERM: Drug Descriptors:
*purine P2Y12 receptor: EC, endogenous compound
*purinergic receptor blocking agent: AE, adverse drug reaction
*purinergic receptor blocking agent: CT, clinical trial
*purinergic receptor blocking agent: CB, drug combination
*purinergic receptor blocking agent: CM, drug comparison
*purinergic receptor blocking agent: DO, drug dose
*purinergic receptor blocking agent: DT, drug therapy
*purinergic receptor blocking agent: PD, pharmacology
*purinergic receptor blocking agent: IV, intravenous drug administration
*purinergic receptor blocking agent: PO, oral drug administration
*purine P2Y12 receptor antagonist: AE, adverse drug reaction
*purine P2Y12 receptor antagonist: CT, clinical trial
*purine P2Y12 receptor antagonist: CB, drug combination
*purine P2Y12 receptor antagonist: CM, drug comparison
*purine P2Y12 receptor antagonist: DO, drug dose
*purine P2Y12 receptor antagonist: DT, drug therapy
*purine P2Y12 receptor antagonist: PD, pharmacology
*purine P2Y12 receptor antagonist: IV, intravenous drug administration
*purine P2Y12 receptor antagonist: PO, oral drug

administration
*antithrombocytic agent: AE, adverse drug reaction
*antithrombocytic agent: CT, clinical trial
*antithrombocytic agent: CB, drug combination
*antithrombocytic agent: CM, drug comparison
*antithrombocytic agent: DO, drug dose
*antithrombocytic agent: DT, drug therapy
*antithrombocytic agent: PD, pharmacology
*antithrombocytic agent: IV, intravenous drug
administration
*antithrombocytic agent: PO, oral drug administration
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
acetylsalicylic acid: PO, oral drug administration
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
clopidogrel: PO, oral drug administration
ticlopidine: CB, drug combination
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
cangrelor: CM, drug comparison
cangrelor: DT, drug therapy
cangrelor: PD, pharmacology
cangrelor: IV, intravenous drug administration
arc 109318xx: DT, drug therapy
arc 109318xx: PD, pharmacology
arc 109318xx: PO, oral drug administration
azd 6140: AE, adverse drug reaction
azd 6140: CT, clinical trial
azd 6140: CB, drug combination
azd 6140: CM, drug comparison
azd 6140: DO, drug dose
azd 6140: DT, drug therapy
azd 6140: PD, pharmacology
azd 6140: PO, oral drug administration
unclassified drug

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) **389574-19-0**

CHEMICAL NAME: Azd 6140; Arc 109318xx

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ACCESSION NUMBER: 2006283984 EMBASE

TITLE: Rebound platelet activation after termination of prasugrel and aspirin therapy due to confirmed non-compliance in patient enrolled in the JUMBO Trial.

AUTHOR: Serebruany V.L.; Midei M.G.; Meilman H.; Malinin A.I.; Lowry D.R.

CORPORATE SOURCE: V.L. Serebruany, HeartDrug Research Laboratories, Osler Medical Center, 7600 Osler Drive, Towson, MD 21204, United States. heartdrug@aol.com
SOURCE: International Journal of Clinical Practice, (2006) Vol. 60, No. 7, pp. 863-866. .
Refs: 16
ISSN: 1368-5031 E-ISSN: 1742-1241 CODEN: IJCPF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jul 2006
Last Updated on STN: 14 Jul 2006

ABSTRACT: Therapy with aspirin and/or adenosine diphosphate (ADP) receptor blockers is associated with better outcomes via inhibition of platelet activity, and subsequent reduction of ischemic vascular events. Non-compliance (NC) is a well-recognised hazard limiting the clinical utility of antiplatelet agents, and, probably worsening outcomes. However, comprehensive platelet characteristics of a confirmed NC patient after acute vascular event have never been reported within a major randomised trial with ADP-receptor antagonists. A 48-year-old male patient, well-educated, was among patients enrolled in the platelet sub-study for the JUMBO trial. He received 325 mg of aspirin daily for 9 months, presented with unstable angina for urgent coronary intervention, and was successfully reperfused with two intracoronary stents. The patient was randomised to a 60 mg prasugrel loading dose, and 10 mg of prasugrel daily for 30 days. Platelets were assessed at baseline, 4 and 24 h, and at 30 days after acute coronary event utilising ADP-, and collagen-induced conventional aggregometry, rapid cartridge-based analyser and flow cytometry. Loading with prasugrel resulted in significant inhibition of platelet activity during and after stenting. However, after assessing platelet biomarkers at 30 days, voluntary withdrawal from the antiplatelet agents was suspected. Based on the platelet activity characteristics, NC was later confirmed, and the patient admitted that he stopped taking both prasugrel and aspirin shortly after discharge due to minor bleeding episodes after shaving. Major platelet activity biomarkers of the index NC patient were compared with those from compliant prasugrel-, clopidogreltreated patients, and healthy controls. The platelet tests uniformly revealed rebound activation by all platelet measures (at least twofold increase) while being especially high for ADP-, and collagen-induced aggregation, platelet/endothelial cell adhesion molecule-1 (PECAM-1), glycoprotein (GP)Ib, GPIIb/IIIa activity, P-selectin, protease activated receptor (PAR)-1 thrombin receptor (activated and intact epitopes), and thrombospondin expression. The clinical benefits of antiplatelet agents are not only denied in NC outpatients, but may put them at additional risk for worsened vascular outcomes due to the rebound platelet activation. Proclaimed 'resistance' to antiplatelet agents may at least in part be a result of NC, especially in the chronic uncontrolled setting. Enforcing compliance will improve outcomes in the clinical trials, and save lives of patients really receiving antiplatelet therapy. .COPYRGT. 2006 The Authors Journal compilation .COPYRGT. 2006 Blackwell Publishing Ltd.

CONTROLLED TERM: Medical Descriptors:
***coronary artery disease: DT, drug therapy**
***coronary artery disease: PC, prevention**
thrombocyte activation
drug withdrawal
patient compliance
drug dose regimen

unstable angina pectoris
flow cytometry
stent
hospital admission
hospital discharge
bleeding: SI, side effect
rebound
protein function
protein expression
human
male
case report
adult
article
priority journal

CONTROLLED TERM: Drug Descriptors:
*prasugrel: AE, adverse drug reaction
*prasugrel: DO, drug dose
*prasugrel: DT, drug therapy
***acetylsalicylic acid: AE, adverse drug reaction**
***acetylsalicylic acid: DO, drug dose**
***acetylsalicylic acid: DT, drug therapy**
adenosine diphosphate
collagen
antithrombocytic agent: AE, adverse drug reaction
antithrombocytic agent: DO, drug dose
antithrombocytic agent: DT, drug therapy
clopidogrel: DT, drug therapy
biological marker: EC, endogenous compound
CD31 antigen: EC, endogenous compound
glycoprotein Ib: EC, endogenous compound
fibrinogen receptor: EC, endogenous compound
PADGEM protein: EC, endogenous compound
proteinase activated receptor 1: EC, endogenous compound
thrombin receptor: EC, endogenous compound
thrombospondin: EC, endogenous compound
heparin: DT, drug therapy
eptifibatide: DT, drug therapy
metoprolol: DT, drug therapy
atorvastatin: DT, drug therapy

CAS REGISTRY NO.: (prasugrel) **389574-19-0**; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (adenosine diphosphate) 20398-34-9, 58-64-0; (collagen) 9007-34-5; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (eptifibatide) 148031-34-9; (metoprolol) 37350-58-6; (atorvastatin) 134523-00-5, 134523-03-8

CHEMICAL NAME: Aspirin

L53 ANSWER 38 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006186415 EMBASE
TITLE: The platelet ATP and ADP receptors.
AUTHOR: Oury C.; Toth-Zsamboki E.; Vermylen J.; Hoylaerts M.F.
CORPORATE SOURCE: M.F. Hoylaerts, Center for Molecular and Vascular Biology, University of Leuven, Herestraat 49, B-3000 Leuven, Belgium. marc.hoylaerts@med.kuleuven.ac.be
SOURCE: Current Pharmaceutical Design, (2006) Vol. 12, No. 7, pp. 859-875. .

Refs: 156
ISSN: 1381-6128 CODEN: CPDEFP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 May 2006
Last Updated on STN: 9 May 2006

ABSTRACT: Adenine nucleotides, ADP and ATP, are coreleased from dense granules during platelet activation, as well as from endothelial cells and damaged red blood cells following vascular injury. Through autocrine and paracrine mechanisms, these extracellular signaling molecules interact with the platelet P2 receptors to amplify ongoing platelet activation. Two receptors for ADP, the G(q)-protein-coupled P2Y(1) and G(i)-protein-coupled P2Y(12) and one receptor for ATP, the P2X(1) ion channel, have been identified on platelets. Due to distinct pharmacological properties and differential regulation, the P2Y and P2X receptors essentially operate on different scales of time and distance and trigger selective intracellular signaling cascades. Recent advances in the understanding of the P2Y receptor physiology have reinforced the concept of these receptors as useful targets for antithrombotic therapy. The function of P2X(1) in platelet activation only recently started to be unraveled. This review focuses on recent findings on the physiology of these platelet ADP and ATP receptors, their distinct downstream intracellular signaling pathways as well as on the available agonists, antagonists and inhibitors that allow their pharmacological discrimination. .COPYRGT. 2006 Bentham Science Publishers Ltd.

CONTROLLED TERM: Medical Descriptors:
protein secretion
thrombocyte activation
endothelium cell
blood vessel injury
signal transduction
hemostasis
thrombosis
protein analysis
protein function
protein localization
artery thrombosis: DT, drug therapy
artery thrombosis: PC, prevention
thrombocyte aggregation inhibition
neutropenia: SI, side effect
thrombocytopenic purpura: SI, side effect
human
nonhuman
review
priority journal
CONTROLLED TERM: Drug Descriptors:
*thrombocyte receptor: EC, endogenous compound
*adenosine triphosphate: EC, endogenous compound
*adenosine diphosphate: EC, endogenous compound
G protein coupled receptor: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
purine P2Y1 receptor: EC, endogenous compound
purine P2X1 receptor: EC, endogenous compound
purine P2X receptor: EC, endogenous compound

purine P2Y receptor: EC, endogenous compound
anticoagulant agent
purine receptor: EC, endogenous compound
ticlopidine: AE, adverse drug reaction
ticlopidine: CM, drug comparison
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
clopidogrel: AE, adverse drug reaction
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
cangrelor
prasugrel: PD, pharmacology
2' deoxy 6 n methyladenosine 3',5' bisphosphate: AN, drug analysis
2' deoxy 6 n methyladenosine 3',5' bisphosphate: DV, drug development
2' deoxy 6 n methyladenosine 3',5' bisphosphate: PD, pharmacology
purinergic receptor blocking agent: AN, drug analysis
purinergic receptor blocking agent: DV, drug development
purinergic receptor blocking agent: PD, pharmacology
2 chloro 6 n methylmethanocarba 2' deoxyadenosine 3',5' bisphosphate: AN, drug analysis
2 chloro 6 n methylmethanocarba 2' deoxyadenosine 3',5' bisphosphate: DV, drug development
2 chloro 6 n methylmethanocarba 2' deoxyadenosine 3',5' bisphosphate: PD, pharmacology
2 propylthio beta gamma dichloromethyleneadenosine triphosphate: AN, drug analysis
2 propylthio beta gamma dichloromethyleneadenosine triphosphate: DV, drug development
2 propylthio beta gamma dichloromethyleneadenosine triphosphate: PD, pharmacology
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
pyridoxal phosphate 6 azophenyl 2',4' disulfonic acid: PD, pharmacology
suramin: AN, drug analysis
suramin: DV, drug development
4,4',4'',4''' (carbonylbis(imino 5,1,3 benzenetriylbis(carbonylimino)))tetrakis benzen 1,3 disulfonic acid: AN, drug analysis
4,4',4'',4''' (carbonylbis(imino 5,1,3 benzenetriylbis(carbonylimino)))tetrakis benzen 1,3 disulfonic acid: DV, drug development
4,4',4'',4''' (carbonylbis(imino 5,1,3 benzenetriylbis(carbonylimino)))tetrakis benzen 1,3 disulfonic acid: PD, pharmacology
unclassified drug
mrs 2279
ar c67085mx
nf 449

CAS REGISTRY NO.: (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (adenosine diphosphate) 20398-34-9, 58-64-0; (ticlopidine) 53885-35-1, 55142-85-3; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (prasugrel) **389574-19-0**; (2' deoxy 6 n methyladenosine 3',5' bisphosphate) 101204-49-3; (acetylsalicylic acid) 493-53-8,

50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (pyridoxal phosphate 6 azophenyl 2',4' disulfonic acid) 149017-66-3; (suramin) 129-46-4, 145-63-1

CHEMICAL NAME: Ar c69931mx; Cs 747; Plavix; Sr 25990c; Mrs 2179; Mrs 2279; Ar c67085mx; Aspirin; Nf 449

L53 ANSWER 39 OF 56 EMBASE

ACCESSION NUMBER: 2006125569 EMBASE

TITLE: Aspirin and clopidogrel resistance: An emerging clinical entity.

AUTHOR: Wang T.H.; Bhatt D.L.; Topol E.J.

CORPORATE SOURCE: D.L. Bhatt, Department of Cardiovascular Medicine, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States. bhattd@ccf.org

SOURCE: European Heart Journal, (2006) Vol. 27, No. 6, pp. 647-654.

Refs: 98

ISSN: 0195-668X E-ISSN: 1522-9645 CODEN: EHJODF

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 28 Mar 2006
Last Updated on STN: 28 Mar 2006

ABSTRACT: Antiplatelet therapy is a cornerstone of cardiovascular medicine. Aspirin and clopidogrel have emerged as critical therapies in the treatment of cardiovascular disease. Despite their efficacy, patients on these medications continue to suffer complications. Millions of patients are currently on low-dose antiplatelet therapy but it is unknown how many of these patients are under-treated or on the wrong medication. Aspirin and clopidogrel resistance are emerging clinical entities with potentially severe consequences such as recurrent myocardial infarction, stroke, or death. The mechanism of resistance remains incompletely defined, but there are specific clinical, cellular, and genetic factors that influence therapeutic failure. These factors range from physicians who fail to prescribe these medications despite appropriate indications to polymorphisms of platelet membrane glycoproteins. Rapid and accurate diagnosis of anti-platelet resistance also remains an issue as new bedside tests are developed. By understanding the mechanism of therapeutic failure and by improving the diagnosis of this clinical entity, a new era of individualized antiplatelet therapy may arise with routine measurements of platelet activity in the same way that cholesterol, blood pressure, and blood sugar are followed, thus improving the care for millions of people. .COPYRGT. The European Society of Cardiology 2005. All rights reserved.

CONTROLLED TERM: Medical Descriptors:
***cardiovascular disease: DR, drug resistance**
***cardiovascular disease: DT, drug therapy**
***cardiovascular disease: PC, prevention**
anticoagulant therapy
heart muscle ischemia: DR, drug resistance
heart muscle ischemia: DT, drug therapy
intracardiac thrombosis: DR, drug resistance
intracardiac thrombosis: DT, drug therapy
acute coronary syndrome: DR, drug resistance
acute coronary syndrome: DT, drug therapy

anticoagulation
blood clot lysis
risk reduction
heart infarction: DR, drug resistance
heart infarction: DT, drug therapy
heart infarction: PC, prevention
recurrent disease: DR, drug resistance
recurrent disease: DT, drug therapy
recurrent disease: PC, prevention
ST segment elevation
stroke: DT, drug therapy
stroke: PC, prevention
coronary artery thrombosis: DT, drug therapy
coronary artery thrombosis: PC, prevention
cardiovascular risk
risk assessment
age distribution
secondary prevention
heart protection
drug treatment failure
drug mechanism
thrombocyte aggregation inhibition
blood pressure
glucose blood level
cholesterol blood level
monotherapy
drug absorption
patient compliance
drug protein binding
congestive heart failure: DT, drug therapy
disease association
hypercholesterolemia
hyperglycemia
drug efficacy
pharmacogenetics
drug megadose
thrombocyte activation
diagnostic test
thrombocyte function
high risk patient
preventive medicine
muscle necrosis: DT, drug therapy
muscle necrosis: PC, prevention
muscle necrosis: SU, surgery
percutaneous coronary intervention
bleeding: SI, side effect
human
clinical trial
review
priority journal

CONTROLLED TERM: Drug Descriptors:
***acetylsalicylic acid: AE, adverse drug reaction**
***acetylsalicylic acid: CT, clinical trial**
***acetylsalicylic acid: CM, drug comparison**
***acetylsalicylic acid: DO, drug dose**
***acetylsalicylic acid: IT, drug interaction**
***acetylsalicylic acid: DT, drug therapy**
***acetylsalicylic acid: PK, pharmacokinetics**
***acetylsalicylic acid: PD, pharmacology**
*clopidogrel: AE, adverse drug reaction

*clopidogrel: CT, clinical trial
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PK, pharmacokinetics
*clopidogrel: PD, pharmacology
antithrombocytic agent: AE, adverse drug reaction
antithrombocytic agent: CT, clinical trial
antithrombocytic agent: CM, drug comparison
antithrombocytic agent: DO, drug dose
antithrombocytic agent: IT, drug interaction
antithrombocytic agent: DT, drug therapy
antithrombocytic agent: PK, pharmacokinetics
antithrombocytic agent: PD, pharmacology
cholesterol: EC, endogenous compound
glucose: EC, endogenous compound
cyclooxygenase 1: EC, endogenous compound
cyclooxygenase 2: EC, endogenous compound
thromboxane b2 receptor: EC, endogenous compound
thromboxane receptor: EC, endogenous compound
cytochrome P450 3A4: EC, endogenous compound
atorvastatin
hydroxymethylglutaryl coenzyme A reductase inhibitor
adenosine diphosphate: EC, endogenous compound
pyridine derivative: CT, clinical trial
pyridine derivative: DT, drug therapy
pyridine derivative: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
azd 6140: CT, clinical trial
azd 6140: CM, drug comparison
azd 6140: DO, drug dose
azd 6140: DT, drug therapy
azd 6140: PO, oral drug administration
azd 6140: PK, pharmacokinetics
azd 6140: PD, pharmacology
purinergic receptor blocking agent: CT, clinical trial
purinergic receptor blocking agent: CM, drug comparison
purinergic receptor blocking agent: DO, drug dose
purinergic receptor blocking agent: DT, drug therapy
purinergic receptor blocking agent: PO, oral drug administration
purinergic receptor blocking agent: PK, pharmacokinetics
purinergic receptor blocking agent: PD, pharmacology
cangrelor: CM, drug comparison
cangrelor: DT, drug therapy
cangrelor: PK, pharmacokinetics
cangrelor: PD, pharmacology
thromboxane receptor blocking agent: AE, adverse drug reaction
thromboxane receptor blocking agent: CT, clinical trial
thromboxane receptor blocking agent: CM, drug comparison
thromboxane receptor blocking agent: DO, drug dose
thromboxane receptor blocking agent: IT, drug interaction
thromboxane receptor blocking agent: DT, drug therapy
thromboxane receptor blocking agent: PK, pharmacokinetics
thromboxane receptor blocking agent: PD, pharmacology
placebo

unclassified drug
CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (cholesterol) 57-88-5; (glucose) 50-99-7, 84778-64-3; (cytochrome P450 3A4) 329736-03-0; (atorvastatin) 134523-00-5, 134523-03-8; (adenosine diphosphate) 20398-34-9, 58-64-0; (prasugrel) **389574-19-0**
CHEMICAL NAME: Aspirin; Cs 747; Ly 640315; Azd 6140

L53 ANSWER 40 OF 56 EMBASE
ACCESSION NUMBER: 2006186052 EMBASE
TITLE: Variable therapeutic effectiveness of clopidogrel in acute coronary syndromes.
AUTHOR: Hepstinstall S.
CORPORATE SOURCE: S. Heptinstall, Cardiovascular Medicine, University of Hospital, Queens Medical Centre, Nottingham NG7 2UH, United Kingdom. s.heptinstall@nottingham.ac.uk
SOURCE: Journal of Thrombosis and Haemostasis, (2006) Vol. 4, No. 3, pp. 539-541. .
Refs: 36
ISSN: 1538-7933 E-ISSN: 1538-7836 CODEN: JTHOA5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2006
Last Updated on STN: 8 May 2006
CONTROLLED TERM: Medical Descriptors:
***acute coronary syndrome: DT, drug therapy**
***acute coronary syndrome: SU, surgery**
drug efficacy
percutaneous coronary intervention
coronary stent
clinical protocol
thrombocyte aggregation
follow up
heart muscle ischemia
thrombosis: CO, complication
thrombosis: DT, drug therapy
thrombosis: PC, prevention
risk assessment
drug dose regimen
drug metabolism
thrombocyte function
maintenance drug dose
human
clinical trial
note
priority journal
CONTROLLED TERM: Drug Descriptors:
*clopidogrel: CT, clinical trial
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
*clopidogrel: PK, pharmacokinetics

acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
ticlopidine: DT, drug therapy
hydroxymethylglutaryl coenzyme A reductase inhibitor
fibrinogen receptor antagonist: DT, drug therapy
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PK, pharmacokinetics
cangrelor: DV, drug development

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) **389574-19-0**

CHEMICAL NAME: Aspirin

L53 ANSWER 41 OF 56 EMBASE

ACCESSION NUMBER: 2006186051 EMBASE

TITLE: High postclopidogrel platelet reactivity in non-ST-elevation acute coronary syndrome treated with stenting: A clue for adverse prognosis?.

AUTHOR: Galvani M.

CORPORATE SOURCE: M. Galvani, Fondazione Cardiologica Sacco, Ospedale Morgagni, Cardiovascular Research Unit, P.zza F.lli Ruffini 6, 47100 Forli, Italy. galvanim@tin.it

SOURCE: Journal of Thrombosis and Haemostasis, (2006) Vol. 4, No. 3, pp. 536-538. .
Refs: 20
ISSN: 1538-7933 E-ISSN: 1538-7836 CODEN: JTHOA5

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Note

FILE SEGMENT: 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
037 Drug Literature Index

LANGUAGE: English

ENTRY DATE: Entered STN: 8 May 2006
Last Updated on STN: 8 May 2006

CONTROLLED TERM: Medical Descriptors:
*ST segment elevation
*thrombocyte activation
***acute coronary syndrome: DT, drug therapy**
***acute coronary syndrome: SU, surgery**
***postoperative thrombosis: CO, complication**
***postoperative thrombosis: DT, drug therapy**
***postoperative thrombosis: PC, prevention**
coronary artery thrombosis: CO, complication
coronary artery thrombosis: DT, drug therapy
coronary artery thrombosis: PC, prevention
anticoagulant therapy
prognosis
coronary stent
coronary artery recanalization
percutaneous coronary intervention
high risk patient
blood sampling
thrombocyte aggregation
recurrent disease: CO, complication

stroke: CO, complication
surgical mortality
thrombocyte aggregation inhibition
reference value
elective surgery
evidence based medicine
human
note
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: CB, drug combination
*clopidogrel: CM, drug comparison
*clopidogrel: DT, drug therapy
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
fibrinogen receptor antagonist: DT, drug therapy
tirofiban: DT, drug therapy
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (tirofiban) 142373-60-2, 144494-65-5, 150915-40-5; (prasugrel) **389574-19-0**

CHEMICAL NAME: Aspirin

L53 ANSWER 42 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006169266 EMBASE
TITLE: Aspirin and clopidogrel resistance.
AUTHOR: Michos E.D.; Ardehali R.; Blumenthal R.S.; Lange R.A.; Ardehali H.
CORPORATE SOURCE: Dr. H. Ardehali, Feinberg Cardiovascular Research Institute, Northwestern University Medical Center, Tarry 12-703, 303 East Chicago Ave, Chicago, IL 60611, United States. h-ardehali@northwestern.edu
SOURCE: Mayo Clinic Proceedings, (2006) Vol. 81, No. 4, pp. 518-526. .
Refs: 77
ISSN: 0025-6196 CODEN: MACPAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2006
Last Updated on STN: 1 May 2006

ABSTRACT: Despite aspirin's and clopidogrel's proven benefit in reducing cardiovascular (CV) events, recurrent CV events still occur in patients receiving antiplatelet therapy. Many of these patients are resistant or only partially responsive to the antiplatelet effects of aspirin and clopidogrel, as determined by standard platelet assays. However, current clinical guidelines do not support routine screening for aspirin or clopidogrel resistance, in part because determination of the most appropriate screening test has not been established. This review attempts to (1) describe the phenomena of clinical aspirin and clopidogrel resistance (ie, treatment failure), (2) discuss the complexity of defining and identifying aspirin and clopidogrel resistance, (3) identify factors that may be responsible for aspirin and clopidogrel resistance, (4) outline several standard platelet function assays and their

limitations, and (5) describe potential new antiplatelet therapies that may benefit aspirin- or clopidogrel-resistant patients. .COPYRGT. 2006 Mayo Foundation for Medical Education and Research.

CONTROLLED TERM: Medical Descriptors:
***cardiovascular disease: ET, etiology**
***thrombosis: DR, drug resistance**
***thrombosis: DT, drug therapy**
recurrent disease
thrombocyte count
practice guideline
screening test
vascular disease: DR, drug resistance
vascular disease: DT, drug therapy
human
clinical trial
meta analysis
systematic review
review

CONTROLLED TERM: Drug Descriptors:
***acetylsalicylic acid: DT, drug therapy**
***acetylsalicylic acid: PD, pharmacology**
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PD, pharmacology
*antithrombocytic agent: DT, drug therapy
*antithrombocytic agent: PD, pharmacology
*thieno[2,3 b]pyridine derivative: DT, drug therapy
*thieno[2,3 b]pyridine derivative: PD, pharmacology
cyclooxygenase 2: EC, endogenous compound
purine P2Y receptor: EC, endogenous compound
adenosine diphosphate: EC, endogenous compound
metoprolol: DT, drug therapy
rifampicin: IT, drug interaction
rifampicin: DT, drug therapy
cilostazol: CT, clinical trial
cilostazol: DT, drug therapy
cilostazol: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
bm 573: CT, clinical trial
bm 573: DT, drug therapy
bm 573: PD, pharmacology
timi 38: CT, clinical trial
timi 38: DT, drug therapy
timi 38: PD, pharmacology
purinergic receptor blocking agent: CT, clinical trial
purinergic receptor blocking agent: DT, drug therapy
purinergic receptor blocking agent: PD, pharmacology
ar 69931mx: CT, clinical trial
ar 69931mx: DT, drug therapy
ar 69931mx: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (adenosine diphosphate) 20398-34-9, 58-64-0; (metoprolol) 37350-58-6; (rifampicin) 13292-46-1; (cilostazol) 73963-72-1; (prasugrel) **389574-19-0**

Searched by Barb O'Bryen, STIC 2-2518

CHEMICAL NAME: Aspirin; Bm 573; Cs 747; Timi 38; Ar 69931mx

L53 ANSWER 43 OF 56 EMBASE

ACCESSION NUMBER: 2006312756 EMBASE
TITLE: Drug Insight: Clopidogrel nonresponsiveness.
AUTHOR: Gurbel P.A.; Tantry U.S.
CORPORATE SOURCE: P.A. Gurbel, Sinai Center for Thrombosis Research, 2401 West Belvedere Avenue, Baltimore, MD 21215, United States. pgurbel@lifebridgehealth.org
SOURCE: Nature Clinical Practice Cardiovascular Medicine, (2006) Vol. 3, No. 7, pp. 387-395. .
Refs: 60
ISSN: 1743-4297 E-ISSN: 1743-4300
PUBLISHER IDENT.: N0602
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Jul 2006
Last Updated on STN: 21 Jul 2006
ABSTRACT: Platelet reactivity to agonists and subsequent activation are important factors that affect the development of atherothrombosis and resultant ischemic events. Pharmacologic intervention with clopidogrel and aspirin during acute **coronary** syndromes and **percutaneous** ***coronary*** intervention is considered the gold standard for attenuating platelet activation and aggregation. Despite significant benefits reported with dual antiplatelet treatment in major clinical trials, the occurrence of adverse ischemic events, including stent thrombosis, remains a serious clinical problem. Nonresponsiveness, also called resistance, to current clopidogrel regimens might play a part in the occurrence of ischemic events. Various mechanisms have been implicated in nonresponsiveness to clopidogrel, including variability in intestinal absorption and hepatic conversion to the active metabolite, drug-drug interactions and receptor polymorphisms. Increased loading and maintenance doses and the use of new and more-potent P2Y(12)-receptor blockers might overcome the phenomenon of clopidogrel nonresponsiveness. The aim of this article is to provide a comprehensive and current review of clopidogrel response variability and nonresponsiveness. .COPYRGT. 2006 Nature Publishing Group.

CONTROLLED TERM: Medical Descriptors:
***acute coronary syndrome: DR, drug resistance**
***acute coronary syndrome: DT, drug therapy**
***acute coronary syndrome: SU, surgery**
***percutaneous coronary intervention**
thrombocyte activation
thrombocyte aggregation inhibition
thrombosis: CO, complication
thrombosis: DT, drug therapy
thrombosis: PC, prevention
drug response
protein polymorphism
maintenance therapy
drug receptor binding
drug mechanism

laboratory test
drug metabolism
drug dose regimen
pharmacodynamics
bleeding: SI, side effect
cerebrovascular accident: CO, complication
cerebrovascular accident: DT, drug therapy
cerebrovascular accident: PC, prevention
heart infarction: CO, complication
heart infarction: DT, drug therapy
heart infarction: PC, prevention
drug bioavailability
drug absorption
human
clinical trial
review
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: AE, adverse drug reaction
*clopidogrel: CT, clinical trial
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PK, pharmacokinetics
*clopidogrel: PD, pharmacology
*clopidogrel: PO, oral drug administration
cytochrome P450 3A4: EC, endogenous compound
rifampicin: IT, drug interaction
Hypericum perforatum extract: IT, drug interaction
erythromycin: IT, drug interaction
atorvastatin: IT, drug interaction
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
purine P2Y12 receptor: EC, endogenous compound
receptor blocking agent: CT, clinical trial
receptor blocking agent: CM, drug comparison
receptor blocking agent: DT, drug therapy
receptor blocking agent: PD, pharmacology
receptor blocking agent: PO, oral drug administration
azd 6140: CT, clinical trial
azd 6140: CM, drug comparison
azd 6140: DT, drug therapy
azd 6140: PD, pharmacology
azd 6140: PO, oral drug administration
cangrelor: CT, clinical trial
cangrelor: CM, drug comparison
cangrelor: DT, drug therapy
cangrelor: PD, pharmacology
cangrelor: PA, parenteral drug administration
prasugrel: AE, adverse drug reaction
prasugrel: CT, clinical trial
prasugrel: CB, drug combination
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology

prasugrel: PO, oral drug administration
unclassified drug
CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (cytochrome P450 3A4) 329736-03-0; (rifampicin) 13292-46-1; (erythromycin) 114-07-8, 70536-18-4; (atorvastatin) 134523-00-5, 134523-03-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (prasugrel) **389574-19-0**
CHEMICAL NAME: (1) Azd 6140; Aspirin
COMPANY NAME: (1) Astra Zeneca (Sweden); Medicines (United States); Lilly (United States); Sankyo (United States)

L53 ANSWER 44 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006229279 EMBASE
TITLE: Antiplatelet therapy: Current strategies and future trends.
AUTHOR: Tantry U.S.; Etherington A.; Bliden K.P.; Gurbel P.A.
CORPORATE SOURCE: Dr. P.A. Gurbel, Sinai Center for Thrombosis Research, 2401 W. Belvedere Ave., Baltimore, MD 21215, United States. pgurbel@lifebridgehealth.org
SOURCE: Future Cardiology, (2006) Vol. 2, No. 3, pp. 343-366. .
Refs: 163
ISSN: 1479-6678 E-ISSN: 1744-8298
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jun 2006
Last Updated on STN: 1 Jun 2006

ABSTRACT: Pharmacological management of thrombotic complications is strongly influenced by antiplatelet treatment strategies. Recent clinical trials have clearly indicated that current antiplatelet strategies may not inhibit recurrent thrombotic events in selected patients and improvement is necessary. Recently, there has been a gradual modification in the guidelines for clopidogrel dosing. In addition, newly developed P2Y(12) receptor inhibitors and thrombin inhibitors are undergoing Phase II and III clinical trials. Moreover, research related to novel agents that interfere with other steps in coagulation and platelet adhesion, and platelet thromboxane and thrombin receptor blockers, show promise. An important future step will probably be the development of personalized therapy based on defining the individual patient's propensity for thrombosis through investigation of platelet-thrombin-fibrin interactions. Such an approach will enhance the targeting of specific therapy based on the pathophysiology of the individual patient. .COPYRGT. 2006 Future Medicine Ltd.

CONTROLLED TERM: Medical Descriptors:
***thrombosis: CO, complication**
***thrombosis: DR, drug resistance**
***thrombosis: DT, drug therapy**
***thrombosis: PC, prevention**
*anticoagulant therapy
***cardiovascular disease: DR, drug resistance**
***cardiovascular disease: DT, drug therapy**
***cardiovascular disease: PC, prevention**
***cardiovascular disease: SU, surgery**

recurrent disease: CO, complication
recurrent disease: DR, drug resistance
recurrent disease: DT, drug therapy
recurrent disease: PC, prevention
practice guideline
drug dose regimen
blood clotting
thrombocyte adhesion
individualization
treatment planning
drug targeting
pathophysiology
drug mechanism
primary prevention
secondary prevention
gastrointestinal hemorrhage: SI, side effect
bleeding: SI, side effect
heart reinfarction: DR, drug resistance
heart reinfarction: DT, drug therapy
heart reinfarction: PC, prevention
systematic review
drug absorption
drug potentiation
human
nonhuman
clinical trial
meta analysis
review
priority journal

CONTROLLED TERM: Drug Descriptors:
*antithrombocytic agent: AE, adverse drug reaction
*antithrombocytic agent: CT, clinical trial
*antithrombocytic agent: CB, drug combination
*antithrombocytic agent: CM, drug comparison
*antithrombocytic agent: DO, drug dose
*antithrombocytic agent: IT, drug interaction
*antithrombocytic agent: DT, drug therapy
*antithrombocytic agent: PK, pharmacokinetics
*antithrombocytic agent: PD, pharmacology
*antithrombocytic agent: PO, oral drug administration
*antithrombocytic agent: PA, parenteral drug administration
clopidogrel: AE, adverse drug reaction
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DO, drug dose
clopidogrel: IT, drug interaction
clopidogrel: DT, drug therapy
clopidogrel: PK, pharmacokinetics
clopidogrel: PD, pharmacology
clopidogrel: PO, oral drug administration
purine P2Y12 receptor: EC, endogenous compound
purinergic receptor blocking agent: CT, clinical trial
purinergic receptor blocking agent: CB, drug combination
purinergic receptor blocking agent: CM, drug comparison
purinergic receptor blocking agent: DT, drug therapy
purinergic receptor blocking agent: PK, pharmacokinetics
purinergic receptor blocking agent: PD, pharmacology
purinergic receptor blocking agent: PO, oral drug administration

Searched by Barb O'Bryen, STIC 2-2518

purinergic receptor blocking agent: PA, parenteral drug administration
thrombin inhibitor: AE, adverse drug reaction
thrombin inhibitor: CT, clinical trial
thrombin inhibitor: CM, drug comparison
thrombin inhibitor: DT, drug therapy
thrombin inhibitor: PD, pharmacology
thromboxane: EC, endogenous compound
fibrin: EC, endogenous compound
thrombin: EC, endogenous compound
heparin: AE, adverse drug reaction
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: CM, drug comparison
heparin: DT, drug therapy
heparin: PD, pharmacology
low molecular weight heparin: AE, adverse drug reaction
low molecular weight heparin: CT, clinical trial
low molecular weight heparin: CB, drug combination
low molecular weight heparin: CM, drug comparison
low molecular weight heparin: DT, drug therapy
low molecular weight heparin: PD, pharmacology
low molecular weight heparin: SC, subcutaneous drug administration
hirulog: AE, adverse drug reaction
hirulog: CT, clinical trial
hirulog: CM, drug comparison
hirulog: DT, drug therapy
hirulog: PD, pharmacology
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: IT, drug interaction
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
anticoagulant agent: CT, clinical trial
anticoagulant agent: CM, drug comparison
anticoagulant agent: DT, drug therapy
anticoagulant agent: PK, pharmacokinetics
anticoagulant agent: PD, pharmacology
anticoagulant agent: PO, oral drug administration
azd 6140: CT, clinical trial
azd 6140: CM, drug comparison
azd 6140: DT, drug therapy
azd 6140: PK, pharmacokinetics
azd 6140: PD, pharmacology
azd 6140: PO, oral drug administration
cangrelor: CT, clinical trial
cangrelor: DT, drug therapy
cangrelor: PK, pharmacokinetics
cangrelor: PD, pharmacology
cangrelor: PA, parenteral drug administration
prasugrel: CT, clinical trial
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
prasugrel: PO, oral drug administration
alteplase: DT, drug therapy
reteplase: DT, drug therapy

tenecteplase: DT, drug therapy
warfarin: CB, drug combination
warfarin: CM, drug comparison
warfarin: DT, drug therapy
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
fibrinogen receptor antagonist: AE, adverse drug reaction
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: CB, drug combination
fibrinogen receptor antagonist: CM, drug comparison
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
abciximab: AE, adverse drug reaction
abciximab: CT, clinical trial
abciximab: CB, drug combination
abciximab: CM, drug comparison
abciximab: DT, drug therapy
abciximab: PD, pharmacology
eptifibatide: AE, adverse drug reaction
eptifibatide: CT, clinical trial
eptifibatide: CB, drug combination
eptifibatide: CM, drug comparison
eptifibatide: DT, drug therapy
eptifibatide: PD, pharmacology
tirofiban: CT, clinical trial
tirofiban: CB, drug combination
tirofiban: CM, drug comparison
tirofiban: DT, drug therapy
tirofiban: PD, pharmacology
fibrinolytic agent: CT, clinical trial
fibrinolytic agent: CB, drug combination
fibrinolytic agent: DT, drug therapy
metoprolol: CT, clinical trial
metoprolol: CB, drug combination
metoprolol: DT, drug therapy
dipyridamole: CB, drug combination
dipyridamole: CM, drug comparison
dipyridamole: DT, drug therapy
dipyridamole: PD, pharmacology
cilostazol: DT, drug therapy
cilostazol: PD, pharmacology
unindexed drug
unclassified drug
arc 669931 mx

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (thromboxane) 66719-58-2; (fibrin) 9001-31-4; (thrombin) 9002-04-4; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (hirulog) 128270-60-0; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (prasugrel) **389574-19-0**; (alteplase) 105857-23-6; (reteplase) 133652-38-7; (tenecteplase) 191588-94-0; (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (ticlopidine) 53885-35-1, 55142-85-3; (abciximab) 143653-53-6; (eptifibatide) 148031-34-9; (tirofiban) 142373-60-2, 144494-65-5, 150915-40-5; (metoprolol) 37350-58-6; (dipyridamole) 58-32-2; (cilostazol) 73963-72-1

CHEMICAL NAME: (1) Azd 6140; (2) Cs 747; (3) Arc 669931 mx; Aspirin; Aggrastat; Reopro; Persantine

COMPANY NAME: (1) Astra Zeneca (United States); (2) Lilly (United

States); (3) Medicines (United States); Sanofi Synthelabo (France)

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ACCESSION NUMBER: 2006090617 EMBASE
TITLE: Regulation of platelet functions by P2 receptors.
AUTHOR: Gachet C.
CORPORATE SOURCE: C. Gachet, Institut National de la Sante et de la Recherche Medicale, Etablissement Francais du Sang-Alsace, Strasbourg 67065, France. christian.gachet@efs-alsace.fr
SOURCE: Annual Review of Pharmacology and Toxicology, (2006) Vol. 46, pp. 277-300. .
Refs: 149
ISSN: 0362-1642 CODEN: ARPTDI
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Mar 2006
Last Updated on STN: 16 Mar 2006

ABSTRACT: The main role of blood platelets is to ensure primary hemostasis, which is the maintenance of vessel integrity and cessation of bleeding upon injury. While playing a major part in acute arterial thrombosis, platelets are also involved in inflammation, atherosclerosis, and angiogenesis. ADP and ATP play a crucial role in platelet activation, and their receptors are potential targets for antithrombotic drugs. The ATP-gated cation channel P2X(1) and the two G protein-coupled ADP receptors, P2Y(1) and P2Y(12), selectively contribute to platelet aggregation and formation of a thrombus. Owing to its central role in the growth and stabilization of a thrombus, the P2Y(12) receptor is an established target of antithrombotic drugs such as clopidogrel. Studies in P2Y(1) and P2X(1) knockout mice and selective P2Y(1) and P2X(1) antagonists have shown that these receptors are also attractive targets for new antithrombotic compounds. The potential role of platelet P(2) receptors in the involvement of platelets in inflammatory processes is also discussed.

CONTROLLED TERM: Medical Descriptors:
*thrombocyte function
*thrombocyte
hemostasis
bleeding
artery thrombosis
inflammation
atherosclerosis
angiogenesis
thrombocyte activation
thrombogenesis
drug targeting
human
nonhuman
clinical trial
review
priority journal
CONTROLLED TERM: Drug Descriptors:
*purine P2 receptor: EC, endogenous compound
adenosine diphosphate: PD, pharmacology

adenosine triphosphate: PD, pharmacology
anticoagulant agent: CT, clinical trial
anticoagulant agent: PD, pharmacology
purine P2X1 receptor: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
clopidogrel: PD, pharmacology
acetylsalicylic acid: PD, pharmacology
prostaglandin synthase inhibitor: PD, pharmacology
ticlopidine: PD, pharmacology
purinergic receptor blocking agent: PD, pharmacology
2' deoxy 6 n methyladenosine 3',5' bisphosphate: PD, pharmacology
mrs 2500: PD, pharmacology
adrenalin: PD, pharmacology
serotonin: PD, pharmacology
suramin: PD, pharmacology
mrs 2279: PD, pharmacology
ar c 66096mx: PD, pharmacology
ar c 67085mx: PD, pharmacology
ar c 69931mx: PD, pharmacology
c 13307: PD, pharmacology
azd 6140: PD, pharmacology
prasugrel: PD, pharmacology
unclassified drug
nf 449

CAS REGISTRY NO.: (adenosine diphosphate) 20398-34-9, 58-64-0; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1, 55142-85-3; (2' deoxy 6 n methyladenosine 3',5' bisphosphate) 101204-49-3; (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (serotonin) 50-67-9; (suramin) 129-46-4, 145-63-1; (prasugrel) **389574-19-0**

CHEMICAL NAME: Mrs 2179; Mrs 2500; Nf 449; Mrs 2279; Ar c 66096mx; Ar c 69931mx; Ar c 67085mx; C 13307; Azd 6140; Cs 747; Ly 640315

L53 ANSWER 46 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006229269 EMBASE

TITLE: A point-of-care assay to measure platelet aggregation in patients taking clopidogrel.

AUTHOR: McLean D.S.; Cannon C.P.

CORPORATE SOURCE: Dr. D.S. McLean, 350 Longwood Ave., Boston, MA 02115, United States. dsmclean@partners.org

SOURCE: Future Cardiology, (2006) Vol. 2, No. 3, pp. 255-267. .
Refs: 75
ISSN: 1479-6678 E-ISSN: 1744-8298

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT:
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 1 Jun 2006

Last Updated on STN: 1 Jun 2006

ABSTRACT: Clopidogrel is an important component of medical therapy for patients with acute coronary syndromes and those receiving coronary stents. Despite the use of clopidogrel, a significant number of patients experience recurrent adverse ischemic events. Inter-individual variability of platelet aggregation in response to clopidogrel may provide an explanation for some of these recurrent events, and small trials have linked clopidogrel resistance, as measured by platelet function tests, to adverse events. The VerifyNow® P2Y12 assay (Accumetrics, Inc., CA, USA) is a point-of-care device that can accurately and rapidly measure the degree of platelet inhibition in patients taking clopidogrel. This assay can identify patients with a poor response to clopidogrel, and could potentially lead to change in therapy. .COPYRGT. 2006 Future Medicine Ltd.

CONTROLLED TERM: Medical Descriptors:
***acute coronary syndrome: DR, drug resistance**
***acute coronary syndrome: DT, drug therapy**
***acute coronary syndrome: SU, surgery**
***acute coronary syndrome: TH, therapy**
*thrombocyte aggregation
*bioassay
drug use
coronary stent
heart muscle ischemia: DI, diagnosis
heart muscle ischemia: ET, etiology
heart muscle ischemia: SI, side effect
individualization
drug response
thrombocyte function
blood clotting parameters
analytical equipment
diagnostic accuracy
drug mechanism
enzyme inhibition
gene activation
drug safety
heart infarction: DT, drug therapy
percutaneous coronary intervention
hematologic disease: SI, side effect
drug dose regimen
thrombosis: CO, complication
bleeding: SI, side effect
coronary artery bypass graft
drug potentiation
human
clinical trial
article
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: AE, adverse drug reaction
*clopidogrel: CT, clinical trial
*clopidogrel: CB, drug combination
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
*clopidogrel: PD, pharmacology
ticlopidine: AE, adverse drug reaction
ticlopidine: CB, drug combination
ticlopidine: CM, drug comparison
ticlopidine: DO, drug dose

ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
prasugrel: PD, pharmacology
adenosine diphosphate: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
purine P2Y1 receptor: EC, endogenous compound
purine P2X receptor: EC, endogenous compound
cyclic AMP: EC, endogenous compound
G protein coupled receptor: EC, endogenous compound
cytochrome P450 3A4: EC, endogenous compound
antithrombocytic agent: AE, adverse drug reaction
antithrombocytic agent: CT, clinical trial
antithrombocytic agent: CB, drug combination
antithrombocytic agent: CM, drug comparison
antithrombocytic agent: DO, drug dose
antithrombocytic agent: DT, drug therapy
antithrombocytic agent: PD, pharmacology
azd 6140: CT, clinical trial
azd 6140: CM, drug comparison
azd 6140: DT, drug therapy
azd 6140: PD, pharmacology
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
creatine kinase: EC, endogenous compound
prostaglandin E1: IT, drug interaction
prostaglandin E1: PD, pharmacology
cangrelor: IT, drug interaction
cangrelor: PD, pharmacology
fibrinogen receptor: EC, endogenous compound
thrombin receptor activating peptide: EC, endogenous compound
unclassified drug

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) **389574-19-0**; (adenosine diphosphate) 20398-34-9, 58-64-0; (cyclic AMP) 60-92-4; (cytochrome P450 3A4) 329736-03-0; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (creatine kinase) 9001-15-4; (prostaglandin E1) 745-65-3; (thrombin receptor activating peptide) 137339-65-2
CHEMICAL NAME: Cs 747; Azd 6140; Ar c69931 mx
NAME OF PRODUCT: (1) VerifyNow P2Y12 assay
COMPANY NAME: (1) Accumetrics (United States)

L53 ANSWER 47 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006324391 EMBASE
TITLE: Gateways to clinical trials.
AUTHOR: Bayes M.; Rabasseda X.; Prous J.R.
CORPORATE SOURCE: M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (2006) Vol. 28, No. 4, pp. 233-277. .
Refs: 259
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Jul 2006
Last Updated on STN: 21 Jul 2006

ABSTRACT: Gateways to Clinical Trials are a guide to the most recent clinical trials in current literature and congresses. The data in the following tables have been retrieved from the Clinical Trials Knowledge Area of Prous Science Integrity®, the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: Adalimumab, adenosine triphosphate, alemtuzumab, alendronate sodium/cholecalciferol, aliskiren fumarate, AMGN-0007, aminolevulinic acid methyl ester, anakinra, anidulafungin, aripiprazole, atomoxetine hydrochloride; Bevacizumab, bosentan; Calcipotriol/β-methasone dipropionate, caldaret hydrate, caspofungin acetate, cetuximab, cinacalcet hydrochloride, clopidogrel, cocaine-BSA conjugate, conivaptan hydrochloride, Cypher; Darbepoetin alfa, delmitide, desloratadine, desmoteplase, desoxyepothilone B, disufenton sodium, DU-176b, duloxetine hydrochloride, dutasteride; EBV-specific CTLs, ecogramostim, edodekin alfa, efalizumab, eletriptan, emtricitabine, entecavir, erlotinib hydrochloride, ertapenem sodium, escitalopram oxalate, etoricoxib, everolimus, ezetimibe; Fanapanel, fondaparinux sodium; Gefitinib, GTI-2040, GW-501516; Her2 E75-peptide vaccine, human insulin; Ibogaine, icatibant acetate, Id-KLH vaccine, imatinib mesylate, immune globulin subcutaneous [human], indacaterol, inolimomab, ipilimumab, i.v. γ-globulin, ivabradine hydrochloride, ixabepilone; Lacosamide, lanthanum carbonate, lenalidomide, levocetirizine, levodopa methyl ester hydrochloride/carbidopa, levodopa/carbidopa/entacapone, lidocaine/ prilocaine; Maraviroc, mecasermin, melevodopa hydrochloride, mepolizumab, mitumomab; Nesiritide; Omalizumab, oral insulin; Parathyroid hormone (human recombinant), patupilone, pegaptanib sodium, PEG-filgrastim, pemetrexed disodium, photochlor, pimecrolimus, posaconazole, prasterone, prasugrel, pregabalin, prilocaine, PRX-00023; QS-21; Ranibizumab, ranirestat, rhodamine 123, rotigaptide; Sarcosine, sirolimus-eluting stent, sitaxsentan sodium, solifenacin succinate, Staphylococcus aureus vaccine; Tadalafil, talactoferrin alfa, talaporfin sodium, Taxus, tecadenoson, tegaserod maleate, telithromycin, temsirolimus, tenofovir disoproxil fumarate, teriparatide, terutroban sodium, tesaglitazar, tesmilifene hydrochloride, TG-100115, tigecycline, torcetrapib; Ularitide; Valproic acid, sodium, voriconazole; Zotarolimus, zotarolimus-eluting stent.

CONTROLLED TERM: Medical Descriptors:
*drug research
anemia: DT, drug therapy
eosinophilia: DR, drug resistance
hypereosinophilic syndrome: DT, drug therapy
neutropenia: DT, drug therapy
hemophilia
angina pectoris: DT, drug therapy
drug eluting stent
cardiovascular disease: DT, drug therapy
cardiovascular disease: TH, therapy
percutaneous transluminal angioplasty
heart infarction: DT, drug therapy
atherosclerosis: DT, drug therapy
coronary artery disease: DT, drug therapy
tachycardia: DT, drug therapy
heart failure: DT, drug therapy
congestive heart failure: DT, drug therapy
hyponatremia: DT, drug therapy

erectile dysfunction: DT, drug therapy
hypertension: DT, drug therapy
granulomatosis: DT, drug therapy
Wegener granulomatosis: DT, drug therapy
vasculitis: DT, drug therapy
ischemia: DT, drug therapy
hypopituitarism: DT, drug therapy
eye allergy: DT, drug therapy
asthma: DT, drug therapy
conjunctivitis: DT, drug therapy
eczema: DT, drug therapy
rhinitis: DT, drug therapy
urticaria: DT, drug therapy
diabetes mellitus: DT, drug therapy
edema
retinopathy
retina macula degeneration
subretinal neovascularization
human
clinical trial
review

CONTROLLED TERM: Drug Descriptors:
recombinant erythropoietin: CT, clinical trial
recombinant erythropoietin: DT, drug therapy
recombinant erythropoietin: SC, subcutaneous drug administration
novel erythropoiesis stimulating protein: CT, clinical trial
novel erythropoiesis stimulating protein: DT, drug therapy
novel erythropoiesis stimulating protein: SC, subcutaneous drug administration
mepolizumab: CT, clinical trial
mepolizumab: DT, drug therapy
mepolizumab: IV, intravenous drug administration
caspofungin: CT, clinical trial
caspofungin: DT, drug therapy
etoricoxib: CT, clinical trial
etoricoxib: DT, drug therapy
etoricoxib: PO, oral drug administration
ivabradine: CT, clinical trial
ivabradine: DT, drug therapy
ivabradine: PO, oral drug administration
atenolol: CT, clinical trial
atenolol: DT, drug therapy
atenolol: PO, oral drug administration
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
prasugrel: CT, clinical trial
prasugrel: CB, drug combination
prasugrel: DT, drug therapy
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: DT, drug therapy
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
heparin: CT, clinical trial
heparin: DT, drug therapy
heparin: IV, intravenous drug administration

rapamycin: CT, clinical trial
rapamycin: DT, drug therapy
cilostazol: CT, clinical trial
cilostazol: CB, drug combination
cilostazol: DT, drug therapy
tecadenoson: CT, clinical trial
tecadenoson: DT, drug therapy
tecadenoson: IV, intravenous drug administration
tg 100115: CT, clinical trial
tg 100115: DT, drug therapy
nesiritide: CT, clinical trial
nesiritide: DT, drug therapy
nesiritide: IV, intravenous drug administration
diuretic agent: CT, clinical trial
diuretic agent: CB, drug combination
diuretic agent: DT, drug therapy
diuretic agent: IV, intravenous drug administration
glyceryl trinitrate: CT, clinical trial
glyceryl trinitrate: CB, drug combination
glyceryl trinitrate: DT, drug therapy
glyceryl trinitrate: IV, intravenous drug administration
placebo
urodilatin: CT, clinical trial
urodilatin: DT, drug therapy
urodilatin: IV, intravenous drug administration
conivaptan: CT, clinical trial
conivaptan: DT, drug therapy
conivaptan: IV, intravenous drug administration
conivaptan: PO, oral drug administration
tadalafil: CT, clinical trial
tadalafil: DT, drug therapy
immunoglobulin: CT, clinical trial
immunoglobulin: DT, drug therapy
immunoglobulin: IV, intravenous drug administration
aliskiren: CT, clinical trial
aliskiren: DT, drug therapy
prasterone: CT, clinical trial
prasterone: DT, drug therapy
levocetirizine: CT, clinical trial
levocetirizine: DT, drug therapy
levocetirizine: PO, oral drug administration
pegaptanib: CT, clinical trial
ranibizumab: CT, clinical trial
unindexed drug
unclassified drug

CAS REGISTRY NO.: (recombinant erythropoietin) 113427-24-0, 122312-54-3, 130455-76-4; (mepolizumab) 196078-29-2; (caspofungin) 189768-38-5; (etoricoxib) 202409-33-4, 202409-40-3; (ivabradine) 148849-67-6, 148870-80-8, 155974-00-8; (atenolol) 29122-68-7; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (prasugrel) **389574-19-0**; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (paclitaxel) 33069-62-4; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (rapamycin) 53123-88-9; (cilostazol) 73963-72-1; (tecadenoson) 204512-90-3; (nesiritide) 124584-08-3, 189032-40-4; (glyceryl trinitrate) 55-63-0; (urodilatin) 115966-23-9; (conivaptan) 168626-94-6, 210101-16-9; (tadalafil) 171596-29-5; (immunoglobulin) 9007-83-4; (aliskiren) 173334-57-1, 173334-58-2, 173399-03-6;

(prasterone) 53-43-0; (levocetirizine) 130018-77-8; (pegaptanib) 222716-86-1; (ranibizumab) 347396-82-1
CHEMICAL NAME: Aspirin; Tg 100115

L53 ANSWER 48 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006229289 EMBASE
TITLE: Clopidogrel resistance: Fact and fiction.
AUTHOR: van Werkum J.W.; Heestermans A.A.C.M.; Deneer V.H.M.; Hackeng C.M.; ten Berg J.M.
CORPORATE SOURCE: J.M. ten Berg, Department of Cardiology, St. Antonius Hospital, PO Box 2500, 3435 CM Nieuwegein, Netherlands. berg03@antonius.net
SOURCE: Future Cardiology, (2006) Vol. 2, No. 2, pp. 215-228. .
Refs: 113
ISSN: 1479-6678 E-ISSN: 1744-8298
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jun 2006
Last Updated on STN: 1 Jun 2006

ABSTRACT: The antiplatelet agent clopidogrel in combination with aspirin has been shown to reduce thrombotic events in patients with acute coronary syndromes and/or who are undergoing **percutaneous coronary** intervention. However, a large interindividual response variability to clopidogrel has been described. The reported rates of inadequate clopidogrel response vary considerably depending on the definition and methodologies used to measure the inhibition of platelet function. Recently, several (small) studies have demonstrated the clinical relevance of an inadequate response to clopidogrel. Moreover, several factors have been associated with a high interindividual variability in response to clopidogrel. These are: dosing, impaired intestinal absorption, cytochrome P450 3A4 and 3A5 activity, drug-drug interactions, polymorphisms of the receptors involved in the process of arterial thrombosis and hemostasis, and the method of measurement of platelet function. Future research for the evaluation of clopidogrel resistance should be based on the assessment of selective P2Y12 receptor inhibition (e.g., the vasodilator-stimulated phosphoprotein-assay or the measurement of stabilization of platelet aggregates) with quick and simple tests. Only then can we reveal the true prevalence and impact of clopidogrel resistance. .COPYRGT. 2006 Future Medicine Ltd.

CONTROLLED TERM: Medical Descriptors:
*drug resistance
thrombosis: DT, drug therapy
thrombosis: PC, prevention
acute coronary syndrome: SU, surgery
percutaneous coronary intervention
drug response
methodology
thrombocyte function
intestine absorption
enzyme activity
genetic polymorphism
artery thrombosis

hemostasis
drug research
protein determination
thrombocyte aggregation
thrombogenesis
drug mechanism
drug dose regimen
drug blood level
drug metabolism
drug antagonism
human
clinical trial
review
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: CT, clinical trial
*clopidogrel: CB, drug combination
*clopidogrel: CR, drug concentration
*clopidogrel: DO, drug dose
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PK, pharmacokinetics
*clopidogrel: PD, pharmacology
*clopidogrel: PO, oral drug administration
antithrombocytic agent: CT, clinical trial
antithrombocytic agent: CB, drug combination
antithrombocytic agent: CR, drug concentration
antithrombocytic agent: DO, drug dose
antithrombocytic agent: IT, drug interaction
antithrombocytic agent: DT, drug therapy
antithrombocytic agent: PK, pharmacokinetics
antithrombocytic agent: PD, pharmacology
antithrombocytic agent: PO, oral drug administration
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
cytochrome P450 3A4: EC, endogenous compound
cytochrome P450 3A5: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
vasodilator stimulated phosphoprotein: EC, endogenous compound
adenosine diphosphate
fibrinogen receptor: EC, endogenous compound
thrombin: EC, endogenous compound
fibrin: EC, endogenous compound
atorvastatin: CB, drug combination
atorvastatin: IT, drug interaction
simvastatin: CB, drug combination
simvastatin: IT, drug interaction
prasugrel: DV, drug development
cangrelor: DV, drug development
purinergic receptor blocking agent: DV, drug development
azd 6140: DV, drug development
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: DT, drug therapy
unclassified drug

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (cytochrome P450 3A4) 329736-03-0; (cytochrome P450 3A5) 336874-97-6; (adenosine diphosphate) 20398-34-9, 58-64-0; (thrombin) 9002-04-4;

(fibrin) 9001-31-4; (atorvastatin) 134523-00-5, 134523-03-8; (simvastatin) 79902-63-9; (prasugrel) **389574-19-0**
CHEMICAL NAME: Aspirin; Azd 6140

L53 ANSWER 49 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006155767 EMBASE
TITLE: Can clopidogrel and aspirin lower mortality in patients with acute myocardial infarction?.
AUTHOR: Bhatt D.L.
CORPORATE SOURCE: Prof. D.L. Bhatt, Cleveland Clinic, Department of Cardiovascular Medicine, 9500 Euclid Avenue, Cleveland, OH 44195, United States. bhattd@ccf.org
SOURCE: Nature Clinical Practice Cardiovascular Medicine, (2006) Vol. 3, No. 4, pp. 182-183. .
Refs: 5
ISSN: 1743-4297 E-ISSN: 1743-4300
PUBLISHER IDENT.: N0508
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Apr 2006
Last Updated on STN: 12 Apr 2006
CONTROLLED TERM: Medical Descriptors:
*mortality
*anticoagulant therapy
***acute heart infarction: DT, drug therapy**
ST segment elevation
questionnaire
patient compliance
cause of death
outcomes research
heart reinfarction: CO, complication
heart reinfarction: DT, drug therapy
heart reinfarction: PC, prevention
stroke: CO, complication
stroke: DT, drug therapy
stroke: PC, prevention
bleeding: SI, side effect
drug safety
drug efficacy
acute coronary syndrome: DT, drug therapy
angiocardiography
thrombocyte aggregation inhibition
brain hemorrhage: SI, side effect
drug targeting
human
clinical trial
short survey
priority journal
CONTROLLED TERM: Drug Descriptors:
*clopidogrel: AE, adverse drug reaction
*clopidogrel: CT, clinical trial
*clopidogrel: CB, drug combination

*clopidogrel: DT, drug therapy
***acetylsalicylic acid: AE, adverse drug reaction**
***acetylsalicylic acid: CT, clinical trial**
***acetylsalicylic acid: CB, drug combination**
***acetylsalicylic acid: DT, drug therapy**
placebo
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: CB, drug combination
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: IV, intravenous drug administration
heparin: DT, drug therapy
low molecular weight heparin: DT, drug therapy
fibrinolytic agent: CB, drug combination
fibrinolytic agent: DT, drug therapy
prasugrel: AE, adverse drug reaction
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
adenosine diphosphate: EC, endogenous compound
receptor blocking agent: AE, adverse drug reaction
receptor blocking agent: CT, clinical trial
receptor blocking agent: DT, drug therapy
receptor blocking agent: PD, pharmacology
azd 6140: AE, adverse drug reaction
azd 6140: CT, clinical trial
azd 6140: DT, drug therapy
azd 6140: PD, pharmacology
cangrelor: AE, adverse drug reaction
cangrelor: CT, clinical trial
cangrelor: DT, drug therapy
cangrelor: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (prasugrel) **389574-19-0**; (adenosine diphosphate) 20398-34-9, 58-64-0

CHEMICAL NAME: Aspirin; Azd 6140

L53 ANSWER 50 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006017817 EMBASE
TITLE: Platelets in atherothrombosis.
AUTHOR: Vorchheimer D.A.; Becker R.
CORPORATE SOURCE: Dr. D.A. Vorchheimer, Zena and Michael Wiener Cardiovascular Institute, Mount Sinai School of Medicine, Box 1030, 1 Gustave Levy Pl, New York, NY 10029, United States. david.vorchheimer@msnyuhealth.org
SOURCE: Mayo Clinic Proceedings, (2006) Vol. 81, No. 1, pp. 59-68.
.
Refs: 89
ISSN: 0025-6196 CODEN: MACPAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Feb 2006
Last Updated on STN: 2 Feb 2006

ABSTRACT: Atherosclerosis is a diffuse, systemic disease that affects the coronary, cerebral, and peripheral arterial trees. Disruption of atherosclerotic plaques leads to thrombus formation and arterial occlusion. This unpredictable and potentially life-threatening atherothrombotic sequence underlies clinical events such as angina, myocardial infarction, transient ischemic attacks, and stroke. One of the key components of a clot is the platelet. Although it was previously thought that platelets were relatively inactive cells that merely provided a framework for the attachment of other cells and proteins to mechanically stop bleeding due to injury, it is now known that this is not the case. Platelets secrete and express a large number of substances that are crucial mediators of both coagulation and inflammation. This article reviews the centrality of the platelet in atherothrombosis and briefly looks at the efficacy of antiplatelet agents in preventing and treating cardiovascular disease. .COPYRGT. 2006 Mayo Foundation for Medical Education and Research.

CONTROLLED TERM: Medical Descriptors:
*thrombocyte
***thrombosis: ET, etiology**
***atherosclerosis: ET, etiology**
*atherothrombosis: ET, etiology
atherosclerotic plaque
thrombogenesis
artery occlusion
disease course
angina pectoris
heart infarction
transient ischemic attack
stroke: SI, side effect
blood clotting
cell adhesion
cell secretion
inflammation
cardiovascular disease: DT, drug therapy
cardiovascular disease: ET, etiology
cardiovascular disease: PC, prevention
drug efficacy
gastrointestinal symptom: SI, side effect
intestine ulcer: SI, side effect
bleeding: SI, side effect
human
clinical trial
review
Drug Descriptors:
antithrombocytic agent: AE, adverse drug reaction
antithrombocytic agent: CT, clinical trial
antithrombocytic agent: DT, drug therapy
antithrombocytic agent: PD, pharmacology
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology

thieno[3,2 c]pyridine derivative: AE, adverse drug reaction
thieno[3,2 c]pyridine derivative: CT, clinical trial
thieno[3,2 c]pyridine derivative: CB, drug combination
thieno[3,2 c]pyridine derivative: DT, drug therapy
thieno[3,2 c]pyridine derivative: PD, pharmacology
clopidogrel: AE, adverse drug reaction
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DO, drug dose
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
metoprolol: CT, clinical trial
metoprolol: CB, drug combination
metoprolol: DT, drug therapy
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: AD, drug administration
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
fibrinogen receptor antagonist: IV, intravenous drug administration
fibrinogen receptor antagonist: PO, oral drug administration
abciximab: DT, drug therapy
abciximab: PD, pharmacology
eptifibatide: DT, drug therapy
eptifibatide: PK, pharmacokinetics
eptifibatide: PD, pharmacology
tirofiban: DT, drug therapy
tirofiban: PK, pharmacokinetics
tirofiban: PD, pharmacology

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) **389574-19-0**; (metoprolol) 37350-58-6; (abciximab) 143653-53-6; (eptifibatide) 148031-34-9; (tirofiban) 142373-60-2, 144494-65-5, 150915-40-5

CHEMICAL NAME: Aspirin

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ACCESSION NUMBER: 2006118487 EMBASE

TITLE: [Molecular target and clinical use of antithrombotic drugs].
FARMACI ANTI-TROMBOTICI. BERSAGLI MOLECOLARI E USO CLINICO.

AUTHOR: Evangelista V.; Totani L.

CORPORATE SOURCE: V. Evangelista, Laboratorio di Biologia e Farmacologia Vascolare, Dipartimento di Epidemiologia Clinica e Farmacologia, Consorzio Mario Negri Sud, S. Maria Imbaro CH

SOURCE: Giornale Italiano di Farmacia Clinica, (2005) Vol. 19, No. 4, pp. 399-407. .
Refs: 14
ISSN: 1120-3749 CODEN: GIFCEN

COUNTRY: Italy

DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Italian
SUMMARY LANGUAGE: English; Italian
ENTRY DATE: Entered STN: 31 Mar 2006
Last Updated on STN: 31 Mar 2006

ABSTRACT: Thrombosis plays a central role in the atherosclerotic process, determining progression and acute ischemic complications. The results of large scale clinical trials demonstrated the efficacy of anti-thrombotic therapies in the acute and chronic treatment of the cardiovascular disease. Anti-platelet and anti-coagulant drugs, alone or together with revascularization procedures such as thrombolysis, **percutaneous coronary** interventions or **coronary** artery by-pass, represent the mainstays of treatment of athero-thrombosis. Available drugs: aspirin, ticlopidine, clopidogrel, dypiridamole and GPIIbIIIa inhibitors, concerning the platelet side; heparin, low molecular weight heparin, direct and indirect inhibitors of factor Xa, thrombin inhibitors and oral anticoagulants, for the coagulation side, target specific molecular mechanisms within the pathways of platelet activation and of the coagulation cascade. Moreover new drugs against new targets are currently tested in preclinical and clinical studies. This brief review summarizes the basic pharmacological mechanisms of the most important anti-thrombotic drugs and, on the basis of recent guidelines, their clinical use.

CONTROLLED TERM: Medical Descriptors:
*drug targeting
thrombosis
atherosclerosis
ischemia: CO, complication
disease course
cardiovascular disease: DT, drug therapy
revascularization
blood clot lysis
percutaneous coronary intervention
coronary artery bypass graft
practice guideline
stroke: DT, drug therapy
human
short survey

CONTROLLED TERM: Drug Descriptors:
*anticoagulant agent: DT, drug therapy
*anticoagulant agent: PD, pharmacology
*anticoagulant agent: PO, oral drug administration
antithrombocytic agent: DT, drug therapy
antithrombocytic agent: PD, pharmacology
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
dipyridamole: DT, drug therapy
dipyridamole: PD, pharmacology
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
heparin: DT, drug therapy
heparin: PD, pharmacology
low molecular weight heparin: DT, drug therapy

low molecular weight heparin: PD, pharmacology
blood clotting factor 10a inhibitor: DT, drug therapy
blood clotting factor 10a inhibitor: PD, pharmacology
thrombin inhibitor: DT, drug therapy
thrombin inhibitor: PD, pharmacology
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
arc 69931rx: DT, drug therapy
arc 69931rx: PD, pharmacology
arc 69931mx: DT, drug therapy
arc 69931mx: PD, pharmacology
abciximab: DT, drug therapy
abciximab: PD, pharmacology
eptifibatide: DT, drug therapy
eptifibatide: PD, pharmacology
tirofiban: DT, drug therapy
tirofiban: PD, pharmacology
2 [4 [(1 acetimidoyl 3 pyrrolidinyl)oxy]phenyl] 3 (7 amidino 2 naphthyl)propionic acid: DT, drug therapy
2 [4 [(1 acetimidoyl 3 pyrrolidinyl)oxy]phenyl] 3 (7 amidino 2 naphthyl)propionic acid: PD, pharmacology
fondaparinux: DT, drug therapy
fondaparinux: PD, pharmacology
idraparinux: DT, drug therapy
idraparinux: PD, pharmacology
antivitamin K: DT, drug therapy
antivitamin K: PD, pharmacology
warfarin: DT, drug therapy
warfarin: PD, pharmacology
blood clotting factor 7a inhibitor: DT, drug therapy
blood clotting factor 7a inhibitor: PD, pharmacology
hirudin: DT, drug therapy
hirudin: PD, pharmacology
hirulog: DT, drug therapy
hirulog: PD, pharmacology
argatroban: DT, drug therapy
argatroban: PD, pharmacology
ximelagatran: DT, drug therapy
ximelagatran: PD, pharmacology
lamifiban: DT, drug therapy
lamifiban: PD, pharmacology
rapamycin
unindexed drug
unclassified drug

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1, 55142-85-3; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (dipyridamole) 58-32-2; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (prasugrel) **389574-19-0**; (abciximab) 143653-53-6; (eptifibatide) 148031-34-9; (tirofiban) 142373-60-2, 144494-65-5, 150915-40-5; (2 [4 [(1 acetimidoyl 3 pyrrolidinyl)oxy]phenyl] 3 (7 amidino 2 naphthyl)propionic acid) 155204-81-2; (fondaparinux) 104993-28-4, 114870-03-0; (idraparinux) 149920-56-9, 162610-17-5; (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (hirudin) 8001-27-2; (hirulog) 128270-60-0; (argatroban) 74863-84-6; (ximelagatran) 192939-46-1, 260790-58-7; (lamifiban) 144412-49-7; (rapamycin) 53123-88-9

CHEMICAL NAME: Arc 69931rx; Arc 69931mx; Dx 9065

L53 ANSWER 52 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006043777 EMBASE
TITLE: Best of TCT 2005.
AUTHOR: Faxon D.P.; Jacobs A.K.; Lepor N.E.; Yeung A.C.
CORPORATE SOURCE: Dr. D.P. Faxon, The University of Chicago Pritzker School of Medicine, Chicago, IL, United States
SOURCE: Reviews in Cardiovascular Medicine, (2005) Vol. 6, No. 4, pp. 214-221. .
ISSN: 1530-6550 CODEN: RCMEC5
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2006
Last Updated on STN: 3 Mar 2006
CONTROLLED TERM: Medical Descriptors:
***cardiovascular disease: DI, diagnosis**
***cardiovascular disease: DT, drug therapy**
***cardiovascular disease: PC, prevention**
***cardiovascular disease: SU, surgery**
***cardiovascular disease: TH, therapy**
drug eluting stent
drug delivery system
coronary stent
angiocardiography
percutaneous coronary intervention
heart infarction: DI, diagnosis
heart infarction: DT, drug therapy
heart infarction: PC, prevention
heart infarction: SU, surgery
heart infarction: TH, therapy
in-stent restenosis: CO, complication
in-stent restenosis: DT, drug therapy
in-stent restenosis: RT, radiotherapy
thrombosis: CO, complication
thrombosis: DT, drug therapy
thrombosis: PC, prevention
angioplasty
coronary artery disease: DI, diagnosis
coronary artery disease: DT, drug therapy
coronary artery disease: PC, prevention
coronary artery disease: SU, surgery
coronary artery disease: TH, therapy
dose response
thrombocyte activation
drug megadose
thrombocyte aggregation inhibition
drug absorption
low drug dose
treatment outcome
stable angina pectoris
ST segment elevation
heart atrium fibrillation
drug contraindication
incidence

cerebrovascular accident
risk assessment
bleeding: SI, side effect
statistical significance
brachytherapy
intermethod comparison
clinical practice
coronary artery bypass surgery
disease severity
atherectomy
heart left ventricle ejection fraction
survival
drug efficacy
follow up
human
clinical trial
review
Drug Descriptors:
polymer
rapamycin
paclitaxel
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: DO, drug dose
clopidogrel: PK, pharmacokinetics
clopidogrel: PD, pharmacology
clopidogrel: PO, oral drug administration
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
heparin: AE, adverse drug reaction
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: DT, drug therapy
heparin: PD, pharmacology
abciximab: CT, clinical trial
abciximab: CB, drug combination
abciximab: CM, drug comparison
abciximab: DT, drug therapy
hirulog: AE, adverse drug reaction
hirulog: CT, clinical trial
hirulog: CB, drug combination
hirulog: DT, drug therapy
warfarin: CT, clinical trial
warfarin: DT, drug therapy
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: CB, drug combination
fibrinogen receptor antagonist: CM, drug comparison
fibrinogen receptor antagonist: DT, drug therapy
tirofiban: CT, clinical trial
tirofiban: CB, drug combination
tirofiban: CM, drug comparison
tirofiban: DO, drug dose
tirofiban: DT, drug therapy
nitinol
politef

CAS REGISTRY NO.: (rapamycin) 53123-88-9; (paclitaxel) 33069-62-4; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (prasugrel) **389574-19-0**; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (abciximab) 143653-53-6; (hirulog) 128270-60-0; (warfarin) 129-06-6,

2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (tirofiban)
142373-60-2, 144494-65-5, 150915-40-5; (nitinol)
52013-44-2; (politef) 9002-84-0, 9039-02-5

L53 ANSWER 53 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006043780 EMBASE
TITLE: Use of antiplatelet agents and anticoagulants for cardiovascular disease: Current standards and best practices.
AUTHOR: Faxon D.P.
CORPORATE SOURCE: Dr. D.P. Faxon, Section of Cardiology, University of Chicago, Chicago, IL, United States
SOURCE: Reviews in Cardiovascular Medicine, (2005) Vol. 6, No. SUPPL. 4, pp. S3-S14. .
Refs: 42
ISSN: 1530-6550 CODEN: RCMEC5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2006
Last Updated on STN: 3 Mar 2006

ABSTRACT: Thrombosis superimposed on arteriosclerosis is the principal cause of mortality and morbidity in patients with arteriosclerosis. The use of antiplatelet agents and anticoagulants in the treatment of arteriosclerosis is well established, based on many large randomized trials. Aspirin is indicated for primary prevention in patients at increased risk of developing symptomatic atherosclerotic vascular disease. For patients with known vascular disease, antiplatelet therapy with aspirin is a well-established treatment. For high-risk patients such as those with acute coronary syndromes (ACS; unstable angina, myocardial infarction), dual antiplatelet therapy with aspirin and clopidogrel is indicated, based on results of the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial. Platelet glycoprotein IIb/IIIa agents are powerful inhibitors of platelet function and are also effective in ACS, but the benefit is confined to high-risk patients. Anticoagulation with heparin or low-molecular-weight heparin (eg, enoxaparin) is also effective, with an approximately 50% reduction in cardiovascular events. These agents are also indicated for patients undergoing ***percutaneous*** **coronary** intervention. Prolonged dual antiplatelet therapy (at least 6 months) is recommended for patients receiving drug-eluting stents. The efficacy of antiplatelet therapy is thus well established in treating atherothrombosis, but aggressive therapy is associated with an increased bleeding risk. Newer agents may provide improved efficacy with a lower risk of bleeding. .COPYRGT. 2005 MedReviews, LLC.

CONTROLLED TERM: Medical Descriptors:
***cardiovascular disease: DT, drug therapy**
***cardiovascular disease: PC, prevention**
practice guideline
good clinical practice
thrombosis: CO, complication
thrombosis: DR, drug resistance
thrombosis: DT, drug therapy
thrombosis: PC, prevention

Searched by Barb O'Bryen, STIC 2-2518

arteriosclerosis: DT, drug therapy
coronary artery disease: DT, drug therapy
acute coronary syndrome: DT, drug therapy
acute heart infarction: DT, drug therapy
unstable angina pectoris: DT, drug therapy
unstable angina pectoris: PC, prevention
mortality
morbidity
treatment indication
primary prevention
atherosclerosis: DT, drug therapy
atherosclerosis: PC, prevention
high risk patient
risk assessment
thrombocyte function
anticoagulation
risk reduction
percutaneous coronary intervention
drug eluting stent
drug efficacy
disease association
bleeding: PC, prevention
bleeding: SI, side effect
cerebrovascular accident: CO, complication
cerebrovascular accident: DT, drug therapy
cerebrovascular accident: PC, prevention
renovascular disease: CO, complication
renovascular disease: DT, drug therapy
renovascular disease: PC, prevention
peripheral vascular disease: CO, complication
peripheral vascular disease: DT, drug therapy
peripheral vascular disease: PC, prevention
disease course
pathophysiology
thrombogenicity
systematic review
thrombocyte aggregation inhibition
antiinflammatory activity
gastrointestinal hemorrhage: SI, side effect
drug megadose
drug safety
drug absorption
drug potency
drug half life
secondary prevention
low drug dose
human
clinical trial
meta analysis
article

CONTROLLED TERM: Drug Descriptors:
*antithrombocytic agent: AE, adverse drug reaction
*antithrombocytic agent: CT, clinical trial
*antithrombocytic agent: CB, drug combination
*antithrombocytic agent: DT, drug therapy
*antithrombocytic agent: PD, pharmacology
*anticoagulant agent: AE, adverse drug reaction
*anticoagulant agent: CT, clinical trial
*anticoagulant agent: CB, drug combination
*anticoagulant agent: CM, drug comparison

*anticoagulant agent: DT, drug therapy
*anticoagulant agent: PK, pharmacokinetics
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
clopidogrel: AE, adverse drug reaction
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DO, drug dose
clopidogrel: DT, drug therapy
clopidogrel: PK, pharmacokinetics
clopidogrel: PD, pharmacology
ticlopidine: AE, adverse drug reaction
ticlopidine: CB, drug combination
ticlopidine: CM, drug comparison
ticlopidine: DO, drug dose
ticlopidine: DT, drug therapy
ticlopidine: PK, pharmacokinetics
ticlopidine: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PK, pharmacokinetics
prasugrel: PD, pharmacology
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: CB, drug combination
fibrinogen receptor antagonist: CM, drug comparison
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PK, pharmacokinetics
fibrinogen receptor antagonist: PD, pharmacology
abciximab: CM, drug comparison
abciximab: DT, drug therapy
abciximab: PK, pharmacokinetics
abciximab: PD, pharmacology
eptifibatide: CT, clinical trial
eptifibatide: CB, drug combination
eptifibatide: CM, drug comparison
eptifibatide: DT, drug therapy
eptifibatide: PD, pharmacology
tirofiban: CT, clinical trial
tirofiban: CB, drug combination
tirofiban: CM, drug comparison
tirofiban: DT, drug therapy
tirofiban: PD, pharmacology
heparin: AE, adverse drug reaction
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: CM, drug comparison
heparin: DT, drug therapy
heparin: PD, pharmacology
low molecular weight heparin: AE, adverse drug reaction
low molecular weight heparin: CT, clinical trial
low molecular weight heparin: CB, drug combination
low molecular weight heparin: CM, drug comparison
low molecular weight heparin: DT, drug therapy

low molecular weight heparin: PK, pharmacokinetics
enoxaparin: AE, adverse drug reaction
enoxaparin: CT, clinical trial
enoxaparin: CM, drug comparison
enoxaparin: DT, drug therapy
enoxaparin: SC, subcutaneous drug administration
dalteparin: DT, drug therapy
blood clotting factor 10a inhibitor: CT, clinical trial
blood clotting factor 10a inhibitor: CM, drug comparison
blood clotting factor 10a inhibitor: DT, drug therapy
blood clotting factor 10a inhibitor: PK, pharmacokinetics
blood clotting factor 10a inhibitor: PD, pharmacology
fondaparinux: CT, clinical trial
fondaparinux: CM, drug comparison
fondaparinux: DT, drug therapy
fondaparinux: PK, pharmacokinetics
fondaparinux: PD, pharmacology
warfarin: AE, adverse drug reaction
warfarin: CT, clinical trial
warfarin: CB, drug combination
warfarin: CM, drug comparison
warfarin: DT, drug therapy
warfarin: PK, pharmacokinetics
warfarin: PO, oral drug administration
thrombin inhibitor: CM, drug comparison
thrombin inhibitor: DT, drug therapy
thrombin inhibitor: PD, pharmacology
hirulog: DT, drug therapy
hirulog: IV, intravenous drug administration
argatroban: DT, drug therapy
argatroban: IV, intravenous drug administration
ximelagatran: DT, drug therapy
ximelagatran: PO, oral drug administration
placebo
fibrinolytic agent: DT, drug therapy
streptokinase: DT, drug therapy
reteplase: CT, clinical trial
reteplase: CB, drug combination
reteplase: DT, drug therapy
tenecteplase: DT, drug therapy
alteplase: DT, drug therapy

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) **389574-19-0**; (abciximab) 143653-53-6; (eptifibatide) 148031-34-9; (tirofiban) 142373-60-2, 144494-65-5, 150915-40-5; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (enoxaparin) 9041-08-1; (fondaparinux) 104993-28-4, 114870-03-0; (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (hirulog) 128270-60-0; (argatroban) 74863-84-6; (ximelagatran) 192939-46-1, 260790-58-7; (streptokinase) 9002-01-1; (reteplase) 133652-38-7; (tenecteplase) 191588-94-0; (alteplase) 105857-23-6

CHEMICAL NAME: Aspirin

L53 ANSWER 54 OF 56 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

Searched by Barb O'Bryen, STIC 2-2518

ACCESSION NUMBER: 2005-778298 [79] WPIX
DOC. NO. CPI: C2005-238563
TITLE: New fused heterocyclic compounds are potassium channel function inhibitors, useful to treat or prevent e.g. arrhythmias, atrial fibrillation, atrial flutter, supraventricular arrhythmias and chronic obstructive pulmonary disease.
DERWENT CLASS: B02 B05
INVENTOR(S): JOHNSON, J A; KOVER, A; LLOYD, J
PATENT ASSIGNEE(S): (JOHN-I) JOHNSON J A; (KOVE-I) KOVER A; (LLOY-I) LLOYD J; (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 110
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 2005250783	A1	20051110	(200579)*		47	A61K031-501
WO 2005105096	A2	20051110	(200579)	EN		A61K031-501

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005250783	A1 Provisional	US 2004-563143P	20040415
		US 2005-104856	20050413
WO 2005105096	A2	WO 2005-US12542	20050414

PRIORITY APPLN. INFO: US 2004-563143P 20040415; US 2005-104856 20050413
INT. PATENT CLASSIF.:
MAIN: A61K031-501
SECONDARY: A61K031-416; A61K031-4172; A61K031-42; A61K031-433; A61K031-517

BASIC ABSTRACT:

US2005250783 A UPAB: 20051208
NOVELTY - Fused heterocyclic compounds (I) and their salts, solvates and prodrugs, are new.

DETAILED DESCRIPTION - Fused heterocyclic compounds of formula (I) and their salts, solvates and prodrugs, are new.

n, m = integers such that ring H, including its fusion partner, is 5-7 membered;

A, B1, D, E = -CR6=, -CR6-, -C(=O)-, -NR7-, -N=, -O-, -S-, bond or double bond;

G (including atoms shared with its fusion partner) = 5-6 membered ring;

R1 = aryl (optionally substituted by one or more -(CH2)p-(Z1)q-(CH2)r-Z2);

R2 = aryl, heteroaryl, cycloalkyl or heterocyclo (all optionally substituted with one or more -(CH2)p-(Z1)q-(CH2)r-Z2) (substituents may join to form an optionally substituted carbocycle or heterocycle);

Y = -C(=O), -C(=S)-, C(=NR9)-, -C(=NR10)NR11-, -C(=O)-O-, - C(=S)-O-,

-C(=NR12), -SO2- or single bond; either
R3-R12 = -(CH2)p-(Z1)q-(CH2)r-Z2; or
two R3-R5 = form optionally substituted carbocycle or heterocycle; or
two R6 = phenyl (optionally substituted); or
R6 and R7 = form optionally substituted carbocycle or heterocycle;
Z1 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo (all optionally substituted), -CZ3Z4-, -O-, -NZ5-, -S-, -SO-, -SO2-, -C(O)-, -C(O)Z6-, -C(O)NZ7-, -C(S)- or -C(=NOZ8)-; either
Z2 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo (all optionally substituted), H, -OZ9, -OC(O)Z10, -NZ11-CO-Z12, -NZ13-CO2-Z14, -NZ15(CO)-NZ16Z17, -NZ18Z19, -NO2, halo, -CN, -C(O)Z20, CO2Z21, -C(S)Z22, -(C=NOZ23)Z24, -C(O)NZ25Z26, -C(S)NZ27Z28, -SZ29, -SOZ30, -SO2Z31 or -SO2NZ32Z33; or
NZ2Z5 = optionally substituted heterocycle;
Z5 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo, heteroaryl, (all optionally substituted), H, -C(O)Z20, -CO2Z21, -C(S)Z22, -(C=NOZ23)Z24, -C(O)NZ25Z26, -C(S)NZ27Z28, -SZ29, -SOZ30, -SO2Z31 or -SO2NZ32Z33;
Z3, Z4, Z6-Z33 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo (all optionally substituted), H or halo; or
(MK#16) p, r = 0-10; and
(MK#17) q = 0-1.
Provided that:
(1) ring G is a heterocycle, where at least one ring atom is nitrogen, and ring G and -C(=O)-, if present, contains at least one unsaturated bond; and
(2) when q is 0, r is also 0.
INDEPENDENT CLAIMS are also included for the following:
(1) a pharmaceutical composition (A) comprising (I), vehicle or carrier; and
(2) preparation of (I).
ACTIVITY - Antiarrhythmic; Gastrointestinal-Gen.; Antiinflammatory; Immunomodulator; Respiratory-Gen.; Antidiabetic; Nootropic; Antimigraine; Anticonvulsant; Hypotensive; Cardiant; Vasotropic; Antianginal; Laxative; Antidiarrheic; Antiasthmatic; Antiarthritic; Antirheumatic; Immunosuppressive; CNS-Gen.; Antiarteriosclerotic; Cytostatic; Ophthalmological; Nephrotropic; Neuroprotective; Antiparkinsonian; Muscular-Gen.; Antiulcer; Auditory; Dermatological; Antiallergic.
MECHANISM OF ACTION - Potassium channel function inhibitor; Ultra-rapidly activating delayed rectifier K+ current blocker. No biological data given.
USE - (I) are useful to treat or prevent arrhythmias, atrial fibrillation, atrial flutter and supraventricular arrhythmias. (I) are useful to treat gastrointestinal disorders (reflux esophagitis or motility disorder), inflammatory, immunological disease (chronic obstructive pulmonary disease), diabetes, cognitive disorder, migraine, epilepsy, hypertension and ultra-rapidly activating delayed rectifier K+ current (I-Kur) associated conditions; and to control heart rate (all claimed). (I) are useful to treat or prevent e.g. diabetes, cognitive disorders, migraine, epilepsy, hypertension, complications of cardiac ischemia, angina pectoris including relief of Prinzmetal's symptoms, vasospastic symptoms and variant symptoms; gastrointestinal disorders including reflux esophagitis, functional dyspepsia, motility disorders (including constipation and diarrhea), and irritable bowel syndrome, asthma, adult respiratory distress syndrome, peripheral vascular disease (including intermittent claudication), venous insufficiency, impotence, inflammatory bowel disease, rheumatoid arthritis, graft rejection, cystic fibrosis, atherosclerosis, restenosis, cancer, auditory system disorder, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, Alzheimer's disease, dementia, central nervous system mediated motor dysfunction

including Parkinson's disease and ataxia; epilepsy; type I diabetes, uveitis, juvenile-onset or recent-onset diabetes mellitus, posterior uveitis, allergic encephalomyelitis, glomerulonephritis, Crohn's disease, ulcerative colitis, migraine, Goodpasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, cutaneous T cell lymphoma, arteriosclerosis, aortitis syndrome, polyarteritis nodosa, myocardosis, scleroderma, Wegener's granuloma and Sjogren's syndrome.

ADVANTAGE - (I) improves cognition in animal models. (I) improves cognition and/or treating cognitive disorders.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-B01; B02-D; B04-C01B; B04-C02E1; B04-C02X; B04-H15; B04-H1500E; B04-L05C; B04-N04A; B05-A03B; B05-B01E; B06-H; B07-H; B10-A08; B10-A17; B10-B02E; B10-C03; B14-C01; B14-C03; B14-C09B; B14-E02; B14-E09; B14-E10; B14-F01A; B14-F01D; B14-F01E; B14-F01G; B14-F02; B14-F07; B14-G02C; B14-G02D; B14-G03; B14-H01; B14-J01; B14-J07; B14-K01; B14-N02; B14-N03; B14-N10; B14-N16; B14-N17; B14-P02; B14-S04; B14-S16

TECH UPTX: 20051208

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (claimed): Preparation of (I) comprises cyclizing a cyclopentane compound of formula (II) via one or more ring-forming reactions to give (I).

J = oxo or -OZ; and

Z = leaving group.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (A) further comprises at least one other therapeutic agent (anti-arrhythmic agent, calcium channel blocker, anti-platelet agent, antihypertensive agent, anti thrombotic/anti thrombolytic agent, anti coagulant, 5-hydroxy-1-methylglutaryl (HMG)-CoA reductase inhibitor, anti diabetic agent, thyroid mimetic, mineralocorticoid receptor antagonist or cardiac glycoside).(A) additionally contains propafenone, carvadiol, propranolol, sotalol, dofetilide, amiodarone, azimilide, ibutilide, diltiazem, verapamil, sulamserod, serraline, tropsetron, dronedarone, diltiazem, verapamil, nifedipine, amlodipine, mybefradil, **aspirin**, indomethacin, ibuprofen, piroxicam, naproxen, celebrex, vioxx, abciximab, eptifibatide, tirofiban, clopidogrel, cangrelor, ticlopidine, **CS-747**, ifetroban, **aspirin**, dipyridamole, chlorothiazide, hydrochlorothiazide, flumethiazide, hydroflumethiazide, bendroflumethiazide, methylchlorothiazide, trichloromethiazide, polythiazide, benzthiazide, ethacrynic acid, tricrynafen, chlorthalidone, furosemide, musolimine, bumetanide, triamtrenene, amiloride, spironolactone, captropril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, lisinopril, losartan, irbesartan, valsartan, sitaxsentan, atrsentan, omapatrilat, gemopatrilat, nitrates, tPA, recombinant tPA, tenecteplase (TNK), lanoteplase (nPA), razaxaban, hirudin, argatroban, streptokinase, urokinase, prourokinase, anisoylated plasminogen streptokinase activator complex, warfarin, heparins (including unfractionated, low molecular weight heparins such as enoxaparin, dalteparin), pravastatin, lovastatin, atorvastatin, simvastatin, NK-104, ZD-4522, squalene, questran, cyclosporin A, taxol, FK 506, adriamycin, epothilones, cisplatin, carboplatin, metformin, acarbose, insulins, repaglinide, glimepiride, glyburide, glipizide, biguanide/glyburide combinations, troglitazone, rosiglitazone, pioglitazone, PPARgamma agonists, aP2 inhibitors, thyrotropin, polythyroid, KB-130015, eplerinone, alendronate, raloxifene, estrogen (including conjugated estrogens in premarin, estradiol),

nefazodone, sertraline, diazepam, lorazepam, buspirone, hydroxyzine pamoate, famotidine, ranitidine, omeprazole, orlistat, digitalis, ouabain, cilostazol, sildenafil, prednisone, dexamethasone or enbrel.

L53 ANSWER 55 OF 56 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-821596 [81] WPIX
DOC. NO. CPI: C2004-285648
TITLE: Treatment or prevention of cardiovascular diseases involves administering 2-acetoxy-5-(alpha-cyclopropylcarbonyl-2-flurorobenzyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridine, and performing **percutaneous coronary** intervention procedure.
DERWENT CLASS: B02
INVENTOR(S): BRANDT, J; FARID, N; JAKUBOWSKI, J; WINTERS, K; BRANDT, J T; FARID, N A; JAKUBOWSKI, J A; WINTERS, K J
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004098713	A2	20041118	(200481)*	EN	31	A61P009-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
EP 1660183	A2	20060531	(200636)	EN		A61P009-00
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PL PT RO SE SI SK TR						

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004098713	A2	WO 2004-US11257	20040426
EP 1660183	A2	EP 2004-750031	20040426
		WO 2004-US11257	20040426

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1660183	A2 Based on	WO 2004098713

PRIORITY APPLN. INFO: US 2003-467903P 20030505
INT. PATENT CLASSIF.:
MAIN: A61P009-00
SECONDARY: A61K031-4365; A61K031-60
BASIC ABSTRACT:
WO2004098713 A UPAB: 20041216
NOVELTY - Treatment or prevention of cardiovascular diseases and their recurrence involves administration of 2-acetoxy-5-(alpha -cyclopropylcarbonyl-2-flurorobenzyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridine (I) optionally in combination with **aspirin**; performing a **percutaneous coronary** intervention (**PCI**) procedure; and optionally administering (I) optionally in

combination with **aspirin.**

DETAILED DESCRIPTION - Treatment or prevention of cardiovascular diseases and their recurrence involves administration of 2-acetoxy-5-(alpha -cyclopropylcarbonyl-2-flurorobenzyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridine (I), its salt, solvate, active metabolite, prodrug, racemate or enantiomer, optionally in combination with **aspirin**; performing a **percutaneous coronary** intervention (**PCI**) procedure; and optionally administering (I) optionally in combination with **aspirin.**

INDEPENDENT CLAIMS are included for the following:

(1) a device coated or impregnated with (I);

(2) use of (I) in conjunction with a **stent** for treating or preventing recurrence of peripheral vascular disease and cerebrovascular disease; and

(3) treatment and prevention of cardiovascular disease and its recurrence involving administering (I), in combination with a **stent** impregnated with (I) and/or other cardio-protective agent.

ACTIVITY - Cardiovascular-Gen.; Vasotropic; Cardiant; Antiinflammatory; Antiarrhythmic.

MECHANISM OF ACTION - None given.

USE - In the manufacture of a medicament for treating or preventing the recurrence of cardiovascular disease e.g. coronary occlusion, restenosis, acute coronary syndrome, high risk vascular diseases, congestive heart failure, cardiac alternation, ventricular aneurysm, mural aneurysm, myocardial infarction, cardiac arrest, cardiac dysrhythmia including atrial fibrillation, cardiac edema, cardiac dyspnea, cardiac failure, tachycardia, cardiac hemoptysis, cardiac incompetence, cardiac murmur, cardiac syncope, cardiac tamponade, cerebrovascular disease and peripheral artery disease (claimed).

ADVANTAGE - The method improves or augments the efficiency of interventional procedures including stenting and balloon angioplasty to minimize recurrences and repeated interventions.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B06-F03; B10-C04B
TECH UPTX: 20041216

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: (m1) involves administration of (I), optionally in combination with **aspirin** or other cardio protective agent to 2 - 30 days prior to performing the **PCI** procedure; performing **PCI** procedure; and administering (I) optionally in combination with **aspirin** or other cardio protective agent to 0 - 365 days after performance of the **PCI** procedure.

L53 ANSWER 56 OF 56 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-482984 [52] WPIX
CROSS REFERENCE: 2000-170974 [15]
DOC. NO. CPI: C2001-144714
TITLE: New biphenyl sulfonamides, useful as angiotensin endothelin receptor antagonists and for treatment of e.g. hypertension, atherosclerosis, asthma and ischemia.
DERWENT CLASS: B05
INVENTOR(S): GU, Z; MACOR, J E; MURUGESAN, N; TELLEW, J E
PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC

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WO 2001044239   A2 20010621 (200152)* EN  286 C07D413-12
   RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
       NL OA PT SD SE SL SZ TR TZ UG ZW
    W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE
       ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
       LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
       SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001020926   A  20010625 (200162)          C07D413-12
EP 1237888      A2 20020911 (200267)  EN      C07D413-12
    R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
       RO SE SI TR
JP 2003520785   W  20030708 (200347)      346 C07D261-10
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APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001044239	A2	WO 2000-US33730	20001213
AU 2001020926	A	AU 2001-20926	20001213
EP 1237888	A2	EP 2000-984282	20001213
		WO 2000-US33730	20001213
JP 2003520785	W	WO 2000-US33730	20001213
		JP 2001-544729	20001213

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001020926	A Based on	WO 2001044239
EP 1237888	A2 Based on	WO 2001044239
JP 2003520785	W Based on	WO 2001044239

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PRIORITY APPLN. INFO: US 2000-643640       20000822; US
                      1999-464037       19991215; US
                      2000-481197       20000111; US
                      2000-513779       20000225; US
                      2000-604322       20000626
INT. PATENT CLASSIF.:
         MAIN:        C07D261-10; C07D413-12
    SECONDARY:        A61K031-42; A61K031-422; A61K031-4245; A61K031-433;
                      A61K031-437; A61K031-4439; A61K031-454; A61K031-4709;
                      A61K031-496; A61K031-497; A61K031-517; A61P003-10;
                      A61P007-00; A61P009-04; A61P009-08; A61P009-10;
                      A61P009-12; A61P011-00; A61P011-06; A61P013-08;
                      A61P013-12; A61P015-10; A61P015-12; A61P025-06;
                      A61P035-00; A61P043-00; C07D261-16; C07D401-12;
                      C07D403-14; C07D413-14; C07D417-12; C07D417-14;
                      C07D471-04; C07D487-04
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BASIC ABSTRACT:

WO 200144239 A UPAB: 20030723

NOVELTY - Biphenyl sulfonamides (I), and their enantiomers, diasteremers, salts and metabolites, are new.

DETAILED DESCRIPTION - Biphenyl sulfonamide compounds of formula (I), and their enantiomers, diasteremers, salts and metabolites, are new.

R1 = a group of formulae (a) - (o);

R2 = T or aryloxy, provided that when R1 is a group of formula (b), that R2 is not H, halo, (halo)alkyl, alkoxy, hydroxyalkyl, nitro, -(CH2)wNR19R20 or -NHSO2R22;

T = H, halo, CHO, (halo)alkyl, alkenyl, alkynyl, (halo)alkoxyalkyl, (cycloalkyl)alkyl, alkoxyalkoxy, cyano, hydroxy(alkyl), nitro,

-CH(OR13)(OR14) or -(CH2)wY
R3 = heteroaryl;
R4, R5 = (hydroxy)alkyl, (hydroxy-substituted)cycloalkyl or (hydroxy-substituted)alkoxyalkyl; or
R4 and R5 together = cyclobutyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl or tetrahydropyranyl (all optionally substituted with one or more OH);
R6 = (hydroxy)(halo)alkyl, (hydroxy-substituted)(cycloalkyl)alkyl, aralkyl, (hydroxy-substituted)alkoxy(alkyl) or -NR16R17;
R7 = -(CH2)w-CO2R15, -(CH2)w-(C=O)NR16R17, -(CH2)w-NR15(C=O)NR16R17, -(CH2)w-CH2OH or -(CH2)w-(C=O)R15, or tetrazolyl, oxadiazolyl or triazolyl (each optionally substituted with H, alkyl, OH or halo);
R8, R9, R9a, R10, R12 = H, halo, (hydroxy)alkyl, (cycloalkyl)(alkyl), (hetero)aryl, arylalkyl, alkylthioalkyl, alkoxy(alkyl); or
R11, R11a = H, alkoxy or together form a carbonyl;
R13, R14 = alkyl or together form a 5- or 6-membered ring;
R15, R16, R17 = H, (hydroxy)alkyl, (cycloalkyl)(alkyl), alkoxyalkyl, aralkyl, heterocycloalkyl, (hetero)aryl or -(CH2)wQ; or
R16 and R17 together = 4-6 membered heterocyclic ring;
n = 1 or 2;
w = 0, 1 or 2;
Y = heteroaryl, -COOH, -COOR18, -CONR19R20, -NR19-OR20, -NR21(C=O)R22, -NR21(C=O)NR19R20, -N(R19)-(alk)-NR21(C=O)R22, -NR21(C=O)OR18, -NR21SO2R22, -SO2R22, or a group of formulae (q), (r) or (s);
R18 - R22 = H, (halo)alkyl, alkoxyalkyl, cycloalkyl, alkenyl, alkynyl, (hetero)aryl or aralkyl; or
R19 and R20 together = 4-7 membered cycloalkyl ring;
R23, R24 = H, (cyclo)alkyl or together form a 3-7 membered ring;
Z = O, -N(R25)- or -C(R26)(R27)-;
x = 2,3 or 4;
R25, R26, R27 = H, (cyclo)alkyl or R26 and R27 together form a 3-7 membered cycloalkyl ring; and
R101 - R104 = T in which all (hetero)aryl rings are optionally substituted by H, halo, cyano, (hydroxy)alkyl, alkoxy, nitro or trifluoromethyl.

Provided that when R1 is a group of formula (a), (I) is not a compound of formula (II).

INDEPENDENT CLAIMS are also included for:

(1) a compound of formula (I) in which R3 = isoxazol-5-yl or isoxazol-3-yl (optionally substituted with 2 of alkyl or halogen, and R1 is any group such that the resulting compound demonstrates affinity (IC50) for both the AT1 receptor and ETA receptor of less than 5 mM at both receptors

(2) a pharmaceutical composition comprising (I), at least one ACE inhibitor (such as captotril, zofenopril, fosinopril, ceranapril, alacepril, enalapril, delapril, pentopril, quinapril, ramipril, or lisinopril), vasopepsidase inhibitor (such as omapatrilat or gemopatrilat), HMG CoA reductase inhibitor (such as pravastatin, lovastatin, atorvastatin, simvastatin, NK-104 or ZD-4522), anti-platelet agent (such as clopidigrel, ticlopidine, **CS-747** or **aspirin**), anti-diabetic agent (such as biguanides or biguanide/glyburide combinations), beta-adrenergic agent (such as carvedilol or metoprolol) or minerocorticoid receptor antagonist (such as spironolactone or eplerenone).

ACTIVITY - Antiarthritic; nootropic; neuroprotective; antianginal; antiarrhythmic; antiarteriosclerotic; antiinflammatory; analgesic; cytostatic; cardiant; cerebroprotective; hepatotropic; dermatological; ophthalmological; antidiabetic; antidiarrheic; anticonvulsant; vasotropic; litholytic; hemostatic; hypotensive; antimigraine; osteopathic;

antipsoriatic; antiulcer.

MECHANISM OF ACTION - Endothelin receptor antagonist; angiotensin II receptor antagonist. Tests were carried out but no results are given.

USE - (I) are useful in the treatment of disorders related to renal, glomerular and mesangial cell function. For treatment of disorders related to paracrine and endocrine function. For treatment of endotoxemia or endotoxin shock or hemorrhagic shock. For alleviating pain associated with prostate and bone cancer. For preventing end-organ damage associated with the cell-proliferative effects of endothelin. For treatment of hypoxic and ischemic diseases (such as cardiac, renal and cerebral ischemia and reperfusion). As antiarrhythmic, antianginal, antifibrillatory, antiasthmatic, antiarteriosclerotic, and antidiarrheal agents. As adjuncts to thrombolytic therapy. For treatment of myocardial infarction, peripheral vascular disease (e.g. Raynaud's disease), cardiac hypertrophy, primary pulmonary hypertension, trauma, central nervous system vascular disorders (such as migraine, stroke and hemorrhage), central nervous system behavioural disorders, gastrointestinal diseases (such as Crohn's disease, ulcers and inflammatory bowel disease), pancreatitis and gall bladder disorders. For regulation of cell growth. For treatment of restenosis following transplantation. For therapy of congestive heart failure including inhibition of fibrosis. For treatment of sickle cell disease, liver disease, deleterious consequences of ET-producing tumors, spastic diseases of the urinary tract and bladder, hepatorenal syndrome, immunological diseases (including vasculitis) fibrosis associated with renal dysfunction, metabolic and neurological disorders, cancer, insulin-retinopathy, diabetes mellitus, neuropathy, retinopathy, epilepsy, bone remodelling, psoriasis, and chronic inflammatory diseases (such as arthritis, rheumatoid arthritis, osteoarthritis, sarcoidosis and eczematous dermatitis). For treatment of disorders involving broncoconstriction. For treatment of sexual dysfunction, Alzheimer's, senile dementia and vascular dementia.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B05-B01E; B06-H; B07-D04B; B07-D09; B07-D13; B10-A08; B10-A17; B10-B02B; B10-C03; B14-C09; B14-E02; B14-E10; B14-F01; B14-F02B; B14-F02C; B14-F02D; B14-F03; B14-F07; B14-G02C; B14-G03; B14-H01; B14-J01; B14-J05D; B14-J07; B14-K01A; B14-K01D; B14-N01; B14-N13; B14-N16; B14-S06; B14-S07

TECH UPTX: 20010914

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can be prepared by:

(1) reacting a sulfonyl-substituted phenyl bromide with an phenyl boronic acid (or ester) to form a biphenyl sulfonyl compound;

(2) converting the biphenyl sulfonyl compound into a biphenyl sulfonyl chloride; and

(3) reacting the biphenyl sulfonyl chloride compound with an aryl amine.

FILE 'HOME' ENTERED AT 11:48:04 ON 10 AUG 2006

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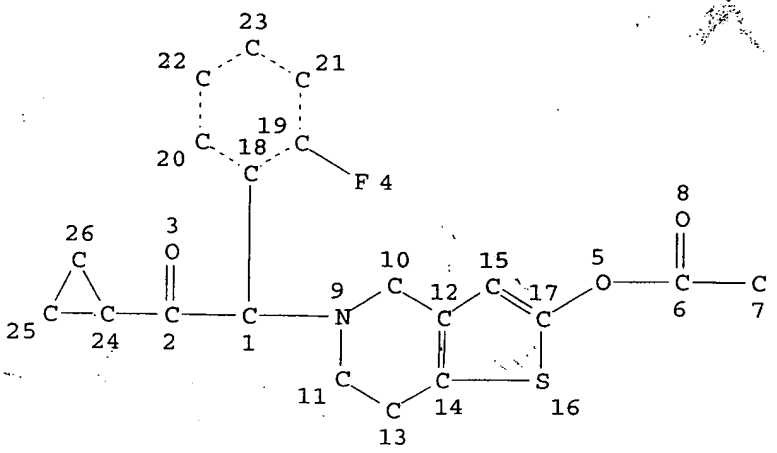
L17 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L19 3 SEA FILE=REGISTRY FAM FUL L17

100.0% PROCESSED 14 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

(FILE 'HOME' ENTERED AT 11:14:07 ON 10 AUG 2006)

FILE 'CAPLUS' ENTERED AT 11:16:02 ON 10 AUG 2006
E US2005-553763/APPS
L1 558 SEA ABB=ON BRANDT J?/AU
L2 152 SEA ABB=ON FARID N?/AU
L3 261 SEA ABB=ON JAKUBOWSKI J?/AU
L4 89 SEA ABB=ON WINTERS K?/AU
L5 2 SEA ABB=ON L1 AND L2 AND L3 AND L4
D SCAN TI
D SCAN
SEL RN

FILE 'REGISTRY' ENTERED AT 11:17:20 ON 10 AUG 2006
L6 10 SEA ABB=ON (115473-15-9/BI OR 150322-38-6/BI OR 150322-43-3/BI OR 150322-73-9/BI OR 204205-33-4/BI OR 389574-19-0/BI OR 389574-20-3/BI OR 446-48-0/BI OR 50-78-2/BI OR 5500-21-0/BI)
D SCAN
L7 1 SEA ABB=ON C20 H20 F N O3 S/MF AND L6
D SCAN

FILE 'STNGUIDE' ENTERED AT 11:19:02 ON 10 AUG 2006

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L8          2404 SEA ABB=ON  BRANDT J?/AU
L9           772 SEA ABB=ON  FARID N?/AU
L10          629 SEA ABB=ON  JAKUBOWSKI J?/AU
L11          371 SEA ABB=ON  WINTERS K?/AU
L12        55838 SEA ABB=ON  PERCUTANEOUS?(5A) CORONARY
L13            3 SEA ABB=ON  L8 AND L9 AND L10 AND L11
L14           16 SEA ABB=ON  (L8 OR L9 OR L10 OR L11) AND L12

     FILE 'CAPLUS' ENTERED AT 11:22:03 ON 10 AUG 2006
                D QUE L5

     FILE 'MEDLINE, JICST-EPLUS, WPIX, BIOSIS, EMBASE' ENTERED AT 11:22:14 ON
     10 AUG 2006
                D QUE L13
                D QUE L14
L15           18 SEA ABB=ON  L13 OR L14

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                     ANSWERS '3-7' FROM FILE MEDLINE
                     ANSWERS '8-13' FROM FILE BIOSIS
                D IBIB ED ABS 1-2
                D IALL 3-13

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                  D LC 1-3

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L20           27 SEA ABB=ON  L19

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L21           61 SEA ABB=ON  L19

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     ENTERED AT 11:26:12 ON 10 AUG 2006
L22           71 DUP REM L20 L21 (17 DUPLICATES REMOVED)
                     ANSWERS '1-27' FROM FILE CAPLUS
                     ANSWER '28' FROM FILE IPA
                     ANSWERS '29-34' FROM FILE BIOSIS
                     ANSWERS '35-67' FROM FILE EMBASE
                     ANSWERS '68-69' FROM FILE TOXCENTER
                     ANSWER '70' FROM FILE IMSRESEARCH
                     ANSWER '71' FROM FILE PROUSDDR

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L23           27 SEA ABB=ON  L19

     FILE 'CAPLUS, IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR' ENTERED AT
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              BI,ABEX
L40        8483 SEA ABB=ON  STENT#/BI,ABEX
L41        4848 SEA ABB=ON  PCI/BI,ABEX OR (PERCUTANEOUS?/BI,ABEX OR PER
              CUTANEOUS?/BI,ABEX OR TRANSLUMINAL?/BI,ABEX OR TRANS LUMINAL?/B
              I,ABEX)(5A)CORONARY/BI,ABEX
L42           9 SEA ABB=ON  L37 AND (L39 OR L40 OR L41)

     FILE 'WPIX' ENTERED AT 11:41:03 ON 10 AUG 2006
              D QUE L42

     FILE 'CAPLUS, IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR, WPIX,
     EMBASE' ENTERED AT 11:41:31 ON 10 AUG 2006
L43           63 DUP REM L34 L23 L42 L33 (22 DUPLICATES REMOVED)
                    ANSWERS '1-26' FROM FILE CAPLUS
                    ANSWER '27' FROM FILE IPA
                    ANSWERS '28-33' FROM FILE BIOSIS
                    ANSWERS '34-35' FROM FILE TOXCENTER
                    ANSWER '36' FROM FILE IMSRESEARCH
                    ANSWER '37' FROM FILE PROUSDDR
                    ANSWERS '38-40' FROM FILE WPIX
                    ANSWERS '41-63' FROM FILE EMBASE

     FILE 'CAPLUS' ENTERED AT 11:42:12 ON 10 AUG 2006
              D SCAN L5

     FILE 'REGISTRY' ENTERED AT 11:42:38 ON 10 AUG 2006
L44            1 SEA ABB=ON  ASPIRIN/CN

     FILE 'CAPLUS' ENTERED AT 11:42:43 ON 10 AUG 2006
L45        20321 SEA ABB=ON  L44
L46         4141 SEA ABB=ON  STENT#/OBI
L47         7059 SEA ABB=ON  (PCI OR (PERCUTANEOUS? OR PER CUTANEOUS? OR
              TRANSLUMINAL? OR TRANS LUMINAL?)(5A)CORONARY)/BI
              D QUE NOS L20
L48           12 SEA ABB=ON  L20 AND (L45 OR L46 OR L47)
L49           15 SEA ABB=ON  L20 NOT (L48 OR L5)
              D SCAN TI
L50            1 SEA ABB=ON  L49 AND COATINGS/TI
              D SCAN
L51            1 SEA ABB=ON  L20 AND COATINGS/TI

     FILE 'CAPLUS' ENTERED AT 11:46:37 ON 10 AUG 2006
              D QUE NOS L48
              D QUE NOS L51
L52           12 SEA ABB=ON  (L48 OR L51) NOT L5

     FILE 'CAPLUS, IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR, EMBASE,
     WPIX' ENTERED AT 11:47:14 ON 10 AUG 2006
L53           56 DUP REM L52 L23 L33 L42 (15 DUPLICATES REMOVED)
                    ANSWERS '1-12' FROM FILE CAPLUS
                    ANSWERS '13-14' FROM FILE IPA
                    ANSWERS '15-23' FROM FILE BIOSIS
                    ANSWERS '24-28' FROM FILE TOXCENTER
                    ANSWER '29' FROM FILE IMSRESEARCH
                    ANSWER '30' FROM FILE PROUSDDR
                    ANSWERS '31-53' FROM FILE EMBASE
                    ANSWERS '54-56' FROM FILE WPIX
                D IBIB ED ABS HITSTR 1-12
                D IALL 13-53
                D IALL ABEQ TECH 54-56
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     11:27:32 ON 10 AUG 2006
L24          38 DUP REM L20 L23 (16 DUPLICATES REMOVED)
                ANSWERS '1-27' FROM FILE CAPLUS
                ANSWER '28' FROM FILE IPA
                ANSWERS '29-34' FROM FILE BIOSIS
                ANSWERS '35-36' FROM FILE TOXCENTER
                ANSWER '37' FROM FILE IMSRESEARCH
                ANSWER '38' FROM FILE PROUSDDR

     FILE 'EMBASE' ENTERED AT 11:27:45 ON 10 AUG 2006
L25          34 SEA ABB=ON  L19
                D TRIAL 1-5
                E CARDIOVASCULAR DISEASE+ALL/CT
L26     1218793 SEA ABB=ON  CARDIOVASCULAR DISEASE+NT/CT
L27       14231 SEA ABB=ON  PCI OR  PERCUTANEOUS?(5A)CORONARY
                D TRIAL 10000-10005
L28       13711 SEA ABB=ON  TRANSLUMINAL CORONARY ANGIOPLASTY/CT
L29          26 SEA ABB=ON  L25 AND (L26 OR L27 OR L28)
                E ASPIRIN/CT
                E E3+ALL
L30       82369 SEA ABB=ON  ACETYLSALICYLIC ACID/CT
                E STENT/CT
                E E3+ALL
L31       27019 SEA ABB=ON  STENT+NT/CT
L32          26 SEA ABB=ON  L25 AND (L30 OR L31)
L33          23 SEA ABB=ON  L25 AND (L30 OR L31) AND (L26 OR L27 OR L28)
                D STAT QUE L19

     FILE 'CAPLUS' ENTERED AT 11:35:07 ON 10 AUG 2006
                D QUE NOS L20
L34          26 SEA ABB=ON  L20 NOT L5

     FILE 'EMBASE' ENTERED AT 11:35:07 ON 10 AUG 2006
                D QUE NOS L33

     FILE 'REGISTRY' ENTERED AT 11:35:12 ON 10 AUG 2006
                D IDE L19 1-3

     FILE 'CAPLUS' ENTERED AT 11:35:20 ON 10 AUG 2006
                D QUE NOS L20
L35          26 SEA ABB=ON  L20 NOT L5

     FILE 'EMBASE' ENTERED AT 11:35:21 ON 10 AUG 2006
                D QUE NOS L33

     FILE 'IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR' ENTERED AT 11:35:41
     ON 10 AUG 2006
                D QUE NOS L23

     FILE 'WPIX' ENTERED AT 11:36:09 ON 10 AUG 2006
                E PRASUGREL/CN
L36           1 SEA ABB=ON  PRASUGREL/CN
                D SDCN DCSE
L37          11 SEA ABB=ON  RA7RM2/DCN OR 199852-0-0-0/DCRE OR PRASUGREL/BI,ABE
                X OR CS747/BI,ABEX OR CS 747/BI,ABEX
                E ASPIRIN/CN
L38           1 SEA ABB=ON  ASPIRIN/CN
                D SDCN DCSE
L39        4469 SEA ABB=ON  R00034/DCN OR R06663/DCN OR 87874-0-0-0/DCRE OR
                ASPIRIN/BI,ABEX OR ACETYLSALICYLIC/BI,ABEX OR ACETYL SALICYLIC/
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FILE 'HOME' ENTERED AT 11:48:04 ON 10 AUG 2006
D STAT QUE L19

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